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AN INTRODUCTION

TO

PATHOLOGY AND MORBID ANATOMY.

AN

INTRODUCTION

TO

PATHOLOGY AND MORBID ANATOMY.

BY

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TO

WILSON FOX, M.D., F.R.S.

PHYSICIAN EXTRAORDINARY TO HER MAJESTY THE QUEEN,
HOLME PROFESSOR OF CLINICAL MEDICINE, FORMERLY PROFESSOR OF
PATHOLOGICAL ANATOMY AT UNIVERSITY COLLEGE, LONDON,
AND PHYSICIAN TO UNIVERSITY COLLEGE HOSPITAL,

THIS SMALL WORK

Is Inscribed

WITH MUCH RESPECT AND GRATITUDE

BY HIS FORMER PUPIL,

THE AUTHOR.

PREFACE.

IN preparing a new edition of his "Introduction to Pathology and Morbid Anatomy," the Author has spared no pains in endeavouring to render it, within its scope, as complete as possible. Although so short a time has elapsed since the first appearance of the work, some of the chapters have been entirely re-written, and such additions and alterations have been made in the various subjects treated of as increased knowledge seemed to demand.

The important subjects of Acute Tuberculosis and Pulmonary Phthisis, which were somewhat briefly alluded to in the former edition, have been treated at much greater length; and a chapter has been added on Pyæmia and Septicæmia. It has also been deemed advisable to append a short chapter on the Preparation and Mounting of Specimens for Microscopical Examination, which it is hoped may increase the usefulness of the work.

Owing to the liberality of his publisher, the Author has been enabled to increase very largely the number of woodcuts. As many as forty new ones have been added.

These have all been drawn by the artist, Mr. Collings, from the Author's preparations. This addition the Author ventures to hope will add in no small degree to the practical utility of the work.

74, Wimpole Street, Cavendish Square,
April, 1873.

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INTRODUCTION.

Pathology treats of the origin, nature, course, and causes of those changes in the body which constitute disease; *Morbid Anatomy*, or *Morbid Histology*, of the actual alterations in the tissues which the disease has produced. The former is therefore comparable with Physiology, the latter with the Histology of the normal tissues.

By *disease* is understood some deviation from the state of health; a deviation consisting for the most part in an alteration in the functions, properties, or structure of some tissue or organ, owing to which its office in the economy is no longer performed in accordance with the normal standard. As *health* is itself merely a relative term and implies no definite performance of the processes of life, so *disease* is equally indefinite; it cannot be separated from health by any well-defined boundary, the one passing by insensible gradations into the other.

Disease is thus, in most cases, merely an abnormal performance of those processes which constitute life, and a knowledge of these processes must therefore necessarily precede the study of pathology. Life comprises the formation and maintenance of the tissues and the exhibition of their various functions. Such formation and maintenance, which may be included under the general term of *Nutrition*, consist in the continuous supply of new material, the separation of this from the blood and its appropriation by the tissues, together with the removal of the products of their waste. *Function* is the special manifestation of the life of the part, as distinct from its growth and the maintenance of its structure; in the secreting cell, consisting in the alteration of the substances abstracted from the blood to fulfil some special purpose in the economy; in nerve, in the transmission of impulses of motion and sensation, &c. The performance of function is obviously dependent upon the state of nutrition. When both of these are normal the condition is one of *health*, when abnormal one of *disease*.

As in health the nutrition is principally dependent upon the tissues themselves, these abstracting, appropriating, and altering the material which is supplied to them by the blood; so in disease it is the *tissues* which play the most important part, and alterations in them are amongst the most frequent of the morbid processes.

The supply and composition of the *blood* must at the same time constitute a most important cause of abnormal nutrition. In regarding the blood, however, as a cause of disease, it must be borne in mind that this fluid is in a state of constant dependence upon other parts; its component elements are derived from external sources and undergo continual change, and although possibly under certain circumstances it may become altered by virtue of changes in the nutritive activity of its corpuscular elements, alterations in its constitution must in most cases result either from some change in the process of its formation, as from the ingestion of improper or insufficient food, mal-assimilation, or disease of the lymphatic structures; from changes in the secretory or excretory processes; or from the introduction of foreign substances, derived from extraneous sources. Whilst, therefore, alterations in the composition of the blood may be important agents in the production of abnormal nutritive changes, they almost invariably depend upon some antecedent condition, and can rarely be regarded as the *primary* cause of disease.

The blood may also play an important part in disease, owing to an abnormal activity of its white corpuscles and their migration through the walls of the blood-vessels into the surrounding tissues. This occurs in the process of inflammation, and probably also in the development of many of the new formations.

Lastly, the influence of the *nervous system* must be taken into account in considering alterations in nutrition and function. This, by regulating the circulation and supply of blood, must to a certain extent control tissue-change. It is probable also that many nerves contain fibres which exercise a direct influence upon nutrition, independently of that which is due to their vaso-motor filaments. Recent anatomical researches, which tend to show that nerve-fibres terminate in the ultimate elements of nearly all tissues, and the rapid atrophy of muscles which often follows certain lesions of the nervous centres and many injuries of the nerve-trunks, render it exceeding probable that such is the case.

The *first* part of this work will be devoted exclusively to the consideration of morbid processes which are characterized mainly by alterations in nutrition; the *second*, to those in which an altered nutrition is associated with certain changes in the blood-vessels and circulation, constituting "inflammation;" and the *third*, to changes in the blood and circulation alone.

CHAPTER I.

THE "CELL."

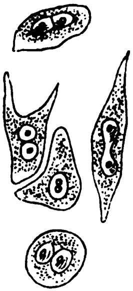
As the most important element in nutrition, both in health and disease, is the activity of the tissues themselves—the supply of nutritive material, although an essential, being merely a *passive* part of the process—it becomes necessary to consider, somewhat minutely, those parts of the tissues in which this activity resides.

Ever since Schwann discovered the cellular nature of animals, and established the analogy between animal and vegetable cells, there has been a gradually increasing conviction amongst physiologists, which has now become an universally accepted physiological and pathological doctrine, that the *cell* is the seat of nutrition and function; and further, that *each individual cell* is itself an independent organism, endowed with all those properties, and capable of exhibiting all those active changes which are characteristic of life. Every organized part of the body is either itself a cell or is derived from cells, and the cells themselves originate from pre-existing cells, and under no circumstances do they originate *de novo.*

Whilst therefore the whole body is made up of cells, or of substances derived from cells, and the cell is itself the ultimate morphological element which is capable of exhibiting any manifestation of life, it must be borne in mind that in a complex organism, the phenomena of life are the result of the continued activity of innumerable cells, many of which possess distinct and peculiar functions, and which by their combination become endowed with new powers, and exhibit new forces; so that, although each individual unit possesses an independent activity, it is in a state of constant dependence upon others with which it is more or less intimately associated.

CONSTITUTION OF CELLS.—When the analogy was established between the animal and vegetable cell, the former was held to be constructed in all cases upon the same principle as the latter, and to consist of a *cell-wall*, enclosing a cavity, in which were contained a *nucleus* and *fluid contents*. (Fig. 1.) This was the idea of the cell held by Schwann and Remak, and supported especially by Virchow, who maintained that these three constituents were essential to its vitality and existence.

FIG. 1.



Cells from a cancer. Showing cell-wall, cell-contents, nuclei, and nucleoli. The nuclei dividing.

During recent years, however, this definition has been modified. The existence of a cell-wall was in many cases not evident. In the embryonic cells, in those of many rapidly growing new formations, and in the corpuscles of blood, pus, and mucus, no limiting membrane could be demonstrated. This led to a new definition of the cell by Leydig and Max Schultze, who held that a little mass of matter enclosing a nucleus was all that was necessary for its constitution, The latter of these physiologists not only rejected the cell-wall as an essential constituent, but established the identity of the mass of matter (cell-contents) with animal sarcode—a contractile substance existing in the lower animals—and showed, that like it, it was endowed with the power of spontaneous movement: this substance he called *protoplasm*. He further pointed out, that the existence of a distinct cell-wall was the result of a retrograde process taking place in the outer layers of the protoplasm, and that the latter was the real seat of the activity of the cell. These views closely correspond with those held by Dr. Beale in this country.*

The definition of a cell has been still further modified by Brücke, Stricker, and others, who consider that the existence of a nucleus is not essential to its constitution. This opinion is principally based upon the fact, that in the cryptogamia, and in some of the lowest animal forms, cells occur in which no nucleus is visible.

It would thus appear probable that a simple mass of protoplasm may, in some exceptional cases, be all that is necessary to constitute a cell—*i.e.*, an elementary organism, capable of exhibiting independently all the phenomena of life; but that the nucleus is an exceedingly constant and almost invariable constituent. The cell-wall is much less constant, and being the result of a retrograde change in the outer layers of the protoplasm, it must be regarded, in point of vitality, as inferior to the rest of the cell.

Protoplasm itself is a homogeneous structureless material, although as it is met with in cells, it often contains adventitious matters—as granules of fat, pigment, &c.—which are either the result of its metamorphosis, or have been taken up from without. In consistence it is subject to constant variations, being sometimes perfectly fluid, at others more or less solid and gelatinous. The cell-wall when it exists, is of much firmer consistence than the protoplasm. In some cells, the protoplasm constitutes but a small proportion of the cell-contents, other substances peculiar to the cell being associated with it; as for example, fat, in the cells of adipose tissue. (See also fatty infiltration of liver cells, Fig. 10.)

---

* Dr. Beale calls the protoplasm, *germinal matter* or *bioplasm*; the cell-wall, *formed material.*

The nucleus is much more constant both in size and form than the cell. It is usually spherical or oval in shape, and often contains one or more minute round or angular bodies, termed *nucleoli*. It offers a greater resistance to chemical reagents than the other constituents of the cell, and in disease often remains after these have been destroyed. It is also stained more deeply by carmine. Structurally, it appears often to be perfectly homogeneous, or faintly granular; in some cases it is invested by a limiting membrane, and is thus of a vesicular nature. Several nuclei may be contained within the same cell.

PHYSIOLOGY OF CELLS.—The cell being, as already stated, the seat of all those nutritive and functional processes which are characteristic of life, the question arises, as to what part is played by its respective constituents, and whether the cell-wall, the protoplasm (cell-contents), and the nucleus have different offices.

The cell-wall being the result of a retrogressive change in the protoplasm, it cannot be regarded as taking any part in the life of the cell, the activity of which is diminished by its existence, as is also its power of reproducing itself by division. It is in old cells that a cell-wall is most frequently met with, in those newly formed it is usually entirely wanting.

The nucleus has always been looked upon as the seat of the nutrition, as distinct from the specific functions of cells, and has been supposed to play an important part in their multiplication and reproduction. The fact that when a cell divides, the division usually commences in the nucleus, and only subsequently takes place in the rest of the cell, would appear to favour this view; as would also the great uniformity of the nucleus both in size and form, whatever be the functional nature of the cell. It must be borne in mind, however, that non-nucleated cells may multiply, and that nucleated cells have been observed to divide, the nucleus itself taking no part in the process.

Whatever be the part played by the nucleus, there can be no doubt that the protoplasm is the most important factor of the cell, and it may itself be the only constituent. The spontaneous movements, alterations in form, and migratory powers characteristic of young cells, are due to the protoplasm. Such movements are observed in the cells of the embryo, in lymphatic and young epithelial cells, in some of the cells of connective tissue, and in white blood-corpuscles and pus-corpuscles.

The protoplasm, as already stated, may be the sole seat of the nutritive and formative power of the cell; it would appear, however, probable that it is especially concerned in the performance of function, and that the specific functional peculiarities of cells are dependent rather upon it than upon their other constituents. The volume and consistence of the protoplasm varies in different cells, and in the same cell, at different times and under different circumstances. It is apparently capable of imbibing and giving up fluids, at the same time undergoing corresponding alterations in volume. These considerations render it probable that it is the seat of the selective power of the cell, and of those other properties which represent its specific functions.

GENESIS OF CELLS.—The proposition of Virchow, that every cell originates directly from a pre-existing cell, forms the basis of the pathology of the present day. To Remak, however, must be ascribed the merit of having first established the cellular origin of the tissues.

The multiplication of cells may take place in three ways—by *simple division*, by *gemmation*, and by *endogenous growth*. In the first two methods the cell breaks up into fragments; in the last, new cells originate within the parent cell. The process is obviously associated with growth and increase of the protoplasm.

The multiplication by simple division is the most frequent method. The cell divides and forms two cells, and each of these again divides and forms two more, and so on. In nucleated cells the nucleus as a rule divides first. The nucleus, however, may divide and multiply within the cell without any division of the cell taking place. If the nuclei multiply within the cell and the protoplasm continuously increase without subsequent division of the cell taking place, large, many-nucleated, irregular-shaped masses of protoplasm are produced. These are the giant or myeloid cells, which are met with in the medulla of young bone, and in some new formations. (See "Myeloid Sarcoma," Fig. 29.) The existence of a dense cell-wall interferes with multiplication by simple division.

In multiplication by gemmation, a small portion of the protoplasm projects from the cell, and becomes detached by constriction at its base, and thus forms a new cell. This is much less frequent than the former process.

Endogenous multiplication occurs principally in cells possessing a dense cell-wall, as in some varieties of epithelium. The protoplasm divides within its limiting membrane, and thus a number of new cells are formed within the parent cell, from which they are subsequently liberated either by the destruction of its wall, or by virtue of their own amœboid activity.*

---

* The author wishes it to be distinctly understood, that in the subsequent pages the term "*cell*" is employed to designate the most elementary factor of the tissues which is capable of exhibiting all the phenomena characteristic of an independent organism, quite irrespectively of the existence of a cell-wall, or even of a nucleus.

CHAPTER II.

NUTRITION ARRESTED.

The absolute and permanent arrest of nutrition constitutes local or systemic death. Under this head are included the three following processes:—

1. *General or Systemic Death.*—In this, the arrest is general; the nutritive processes cease throughout the whole body.

2. *Gangrene or Necrosis.*—The arrest is local, and confined to a particular part, which, when dead, retains to a greater or less extent its external form and anatomical characters.

3. *Molecular Death or Necrobiosis.*—The arrest is also local, but usually results from a previous gradual impairment of the nutritive processes, which ultimately entirely cease in some of the histological elements. The dead part is a granular débris in which all trace of the original structure is lost. This will be considered under "Atrophy and Degeneration."

GANGRENE OR NECROSIS.

Gangrene or Necrosis is the complete and permanent arrest of nutrition in a part—occurring for the most part more or less suddenly—which, when dead, retains to a greater or less extent its external form and anatomical structure. The series of processes by which this is brought about is called *Mortification*, the dead tissue—a *Sphacelus* or *Slough*. In bone the process is called *Necrosis*, the result—a *Sequestrum*.

The arrest of nutrition is followed by the complete cessation of all the evidences of life both functional and physical; and the part thus removed from the influence of the "vital forces" undergoes those chemical and physical changes which are common to inanimate organic matter. In a limb, for example, there is paralysis of motion and sensation, coldness, dryness of the surface; the natural firmness and elasticity are lost, and it becomes soft and doughy, the colouring matter escapes from the blood-corpuscles, and dissolved in the liquor sanguinis permeates and stains the tissues. Evaporation from the surface is to a great extent hindered by the epidermis, consequently, if the limb contains much blood, the transuded serum and the watery constituents of the tissues often form large bullæ on the surface. As decomposition proceeds, gases are generated in the part;—principally sulphuretted hydrogen, ammonia, nitrogen, and carbonic acid: these give rise to the emphysematous crackling which is so often associated with the gangrenous process. The tissues at the same time undergo a process of softening or liquefaction, the limb becomes exceedingly offensive, and changes from a reddish colour to a brownish or greenish-black. This is owing to changes in the transuded hæmoglobin. If the limb does not contain a large amount of blood, and evaporation is allowed to go on freely from the surface by the destruction of the epidermis and rupture of the bullæ, it may dry up—the process of decomposition gradually ceasing—and become converted into a black shrunken mass, which undergoes but little further change :—this constitutes *Dry Gangrene* or *Mummification.* If, on the other hand, as is more commonly the case, the gangrene is associated with venous obstruction, and thus the return of blood and absorption of fluids are prevented, the evaporation from the surface is rarely sufficient to dry the limb, and consequently, the process of decomposition proceeds until it is completely disorganized :—this is *Moist Gangrene.*

The characters of the dead part vary with its structure, its vascularity, the cause of the gangrene, the acuteness of the process, and the possibility of the access of atmospheric air. The more vascular the tissue, the softer its structure, and the more it is exposed to the atmosphere, the more rapidly and completely does it undergo decomposition. Bone, cartilage, and tendons, which are firm hard tissues, containing comparatively but few vessels, undergo very little alteration in structure and form; whereas softer parts are much more rapidly and completely destroyed.

The occurrence of decomposition manifests itself in the first place in the blood contained in the part: this fluid undergoes the earliest and most rapid change. The hæmoglobin escapes from the red corpuscles, partly by exudation, and partly by the destruction of the corpuscles themselves, and dissolved in the liquor sanguinis permeates the surrounding tissues. The corpuscles are ultimately completely annihilated, nothing remaining but a few minute granules.

The staining of the tissues with hæmoglobin, commonly known as *post mortem staining,* is very characteristic. All the tissues are more or less affected, the lining membrane of the blood-vessels, which is in immediate contact with the blood, being naturally more so than other parts. The staining is of an uniform pinkish-red colour, thus differing from the punctiform and stratiform redness of hyperæmia, from which it must be carefully distinguished. The amount of staining is in proportion to the rapidity with which decomposition has taken place, and to the amount of blood contained in the part at the time of death. It is usually most marked in the lining membrane of the heart and large blood-vessels.

Rigor Mortis.—In muscle the arrest of nutrition is accompanied by a state of rigidity, known as the *Rigor Mortis.* This is a peculiar condition of the muscles observed in almost all bodies after death, in which they become firm and somewhat shortened, as though in a state of chronic contraction. It comes on as soon as the muscles have lost their irritability, *i.e.* their capability of responding to artificial stimulation; in other words, as soon as the nutritive processes have completely ceased. The time of its appearance will therefore depend upon the state of nutrition of the muscles at the time of death; the more healthy and vigorous this is, the longer it is before it completely ceases, and consequently the longer it is before the rigor mortis supervenes. The length of its duration and its intensity are in direct proportion to the lateness of its appearance. In people, for example, who are in perfect health, and die suddenly, as from accident, the rigor mortis does not usually come on until from ten to twenty-four hours after death; it is very marked, and often lasts two or three days. In those, on the other hand, who die from some exhausting disease, as from chronic phthisis or the adynamic fevers, in which the nutrition of the muscles becomes much impaired, the rigor mortis appears very soon, sometimes only ten minutes after death; it is very slight and may pass off in less than an hour. It has been said that in cases of death from poisoning by carbonic acid and sulphuretted hydrogen, from lightning, and from some of the severer forms of the adynamic fevers, the rigor mortis is entirely absent. It is doubtful, however, if this is the case, as the rigor mortis has probably escaped observation, owing to its early supervention and rapid disappearance. As soon as the rigor mortis has passed off, decomposition of the muscular tissue commences.

The rigor mortis occurs not only as the result of systemic and local death, but it may also be induced artificially by temporarily arresting the nutrition of the muscle. If the supply of blood to a muscle be cut off by the application of a ligature to the artery supplying it, it quickly passes into a condition which is indistinguishable from the rigor mortis. If the ligature be removed sufficiently early this disappears, and the vitality of the muscle is restored.

With regard to the nature of the change—it was formerly supposed to be a spontaneous contraction, the last act of vitality on the part of the muscle. More recently, however, Kühne and others have shown that it is really owing to the presence of a firm albuminoid compound (Myosin), which is separated from the fluid of the muscle when its nutrition has ceased and coagulates in its substance, thus causing the firmness, hardness, and opacity, which disappear as soon as its disintegration and decomposition commence. The transverse striation of the fibres then becomes indistinct and gives place to irregular rows of granules and fat molecules, the muscle softens, its sarcolemma is destroyed, and ultimately nothing remains but a soft structureless débris.

A similar coagulation appears to take place in the cells of plain involuntary muscle, and here also a rigor mortis occurs. In the cells of other tissues—as the Malpighian layer of the skin, the connective tissues, and glandular organs—a coagulation of the protoplasm has been observed on the cessation of the nutritive processes; the cells become cloudy and granular, and then break up into molecules of various sizes.

Respecting the disintegration of other tissues:—The cells of adipose tissue rapidly diminish in size, owing to the escape of the fluid fat which diffuses itself throughout the surrounding structures. The fibres of connective tissue swell up, become opaque, and ultimately liquefy. In nerve-fibres, the white substance of Schwann coagulates and collects into small drops (myeline) within the neurilemma. Cartilage and bone resist the necrotizing process longer than any of the tissues and are the least altered by it.

The termination of the gangrenous process varies. It may, after involving a greater or less extent of tissue, become arrested, and a "line of demarcation" form between the dead and living parts (*Circumscribed Gangrene*); or the process may continue to extend without any such attempt at recovery (*Diffuse Gangrene*). When the process becomes arrested, the dead tissue—the sphacelus or slough—acts as a foreign body, and as such sets up inflammatory changes in the adjacent structures, and by this means it is ultimately removed or becomes encapsuled. The tissues immediately surrounding the necrosed part are thus in a state of inflammation, as is evidenced in external structures by their swelled condition, red colour, and high temperature. As the gangrenous process ceases, the necrosed fragment becomes limited by this line of inflamed tissue, which constitutes the "*line of demarcation*" between the dead and living parts. Along this line a process of ulceration and suppuration takes place, and by means of this the dead mass is gradually separated from the surrounding structures. The ultimate termination of the process depends principally upon the situation of the affected part:—if this be superficial the slough is thrown off, as in external parts, the intestines, the pharynx, &c., an ulcerated surface being left. If the dead mass is deeply seated, its removal becomes possible only by the extension of the necrotizing process to the surface, as is exemplified by the spontaneous removal of necrosed bone through fistulous openings in the soft parts, and by the opening of an abscess. In other cases the inflammatory process which takes place in the tissues surrounding the dead part is less intense, and the formation of pus is less abundant and is soon followed by that of connective tissue, a layer of which is ultimately formed around the necrosed mass by which it becomes *encapsuled*. This occurs especially in internal parts; examples of it are furnished by foreign bodies, masses of tubercle, hæmorrhagic infarcts, accumulated epithelial products, portions of necrosed bone, and a fœtus in the abdominal cavity, all of which may thus become surrounded by a layer of connective tissue. The part when thus encapsuled is usually rendered inert and no longer acts as an irritant to the tissues in which it lies; it undergoes a gradual process of absorption and drying up, and often becomes calcified.

CAUSES.—The causes of gangrene may be divided into those which interfere with the supply of nutritive material, and those which directly destroy the vitality of the histological elements so that they are no longer able to perform their functions.

A. The supply of nutritive material may be interfered with by:—

1. *Obstruction in the Arteries.*—This is a common cause of gangrene. The obstruction may be caused by a ligature, by compression of the vessel, by solution of its continuity, by thrombosis or embolism, and by disease of the arterial coats. If the obstruction be complete and a collateral circulation cannot be established, death of the part quickly ensues. Obstruction to the arteries alone, the return of blood by the veins not being interfered with, usually produces the dry form of gangrene.

2. *Obstruction in the Capillaries.*—Obstruction here is usually the result of pressure upon or stretching of the vessels. This may take place from the accumulation of inflammatory products, hæmorrhage, or from the pressure exercised by new growths; the resulting obstruction to the capillary circulation causing the death of the immediately adjacent tissues. As examples of gangrene from this cause may be mentioned the necrosis of the superficial layers of the bone which so frequently results from periostitis, owing to the compression of the capillaries between the bone and the periosteum; also the sloughing of the mucous membranes in diphtheria.

3. *Obstruction in the Veins.*—Obstruction to the return of blood by the veins must be so complete in order to arrest nutrition, that it is in itself rarely a cause of gangrene. It is when associated with obstruction in the arteries that it constitutes an important agent in producing this result. This combination of venous and arterial obstruction is seen in a strangulated hernia, in the invagination of a portion of the intestine, in the constriction of a part by a tight bandage, and in contusions and lacerations of the soft parts in which both arteries and veins are injured or become strangulated by the tension of the tissues which subsequently ensues. In all cases in which gangrene is associated with venous obstruction it is of the *moist* variety.

4. *Diminished Cardiac Power.*—This, like venous obstruction, is seldom independently a cause of gangrene. In cases, however, of excessive general debility or disease of the cardiac substance, the consequent diminution in the contractile power of the heart materially aids the foregoing causes in producing a fatal blood-stasis. The arrest of the circulation in "senile gangrene," and that which so often occurs in the tissues of the back in adynamic fevers and in chronic exhausting diseases, is in part the result of diminished cardiac power. This arrest, in the last-named conditions, is usually determined by some injurious stimulation of the tissue—in other words, it is a part of an inflammatory process.

5. *Inflammation.*—The effect of the inflammatory process is to impede or arrest the circulation, and to impair the vitality of the affected part, and the intensity of the process may be so great as to permanently arrest the circulation and cause gangrene. Gangrene from inflammation has been called *inflammatory*, *acute*, or *hot* gangrene. It is always of the moist variety, and is characterized by the heat, swelling, tension, and redness of the affected part, which quickly becomes flaccid, cold, of a greenish-black colour, and ex-

hales an offensive odour. Certain inflammations have a special tendency to terminate in gangrene, as diphtheria, erysipelas, carbuncle, and "hospital gangrene." In all cases, the more impaired the nutrition of the part which becomes the seat of an inflammatory process, the more likely is this to cause its death.

B. Destruction of the vitality of the histological elements may be caused by:—

1. *Mechanical Agencies.*—Under this head are included external violence, heat, cold, and corrosive substances, all of which, by directly and completely destroying vitality, may be causes of gangrene. In most cases, however, this result is preceded by more or less inflammation.

2. *Poisons introduced into the Circulation.*—Phosphorus and ergot of rye are the most important of these. The necrosis of the jaw which results from phosphorus appears, however, to be owing to the direct contact of the phosphorus with the bone, and the gangrene of the extremities which sometimes follows the long continued ingestion of ergot, is probably due to that contraction of the small arteries which this substance produces.

SENILE GANGRENE.—This is a form of mortification which affects especially the lower extremities of old people, and is the result of several of those conditions which have already been enumerated as causes of angrene.

The most important element in the production of senile gangrene consists in the occurrence of atheromatous or calcareous changes in the arteries of the limb, in consequence of which the circulation in it becomes impeded and its vitality impaired. This is evidenced by the coldness of the feet, the cramps, and the other abnormal sensations which are so often experienced by the patient some time before the gangrene sets in. This tendency to local stagnation of the circulation is usually materially increased by the simultaneous atrophy or degeneration of the muscular substance of the heart itself. The combined effect of the diminished *vis à tergo* and of the arterial degeneration may, in some cases, be alone sufficient to cause arrest of the circulation and the formation of thrombi in the vessels of the limb, and thus to cause gangrene. The supervention of the gangrene, however, is usually determined by some injurious stimulation of the tissue, as a slight abrasion of the foot, a bruise, injury to a corn, or excess of heat or cold, which sets up inflammation in the already weakened part, and thus by still further obstructing the circulation in it, and impairing its vitality, causes its death. Senile gangrene is usually of the *dry* variety.

CHAPTER III.

NUTRITION IMPAIRED.

It has been seen in the preceding chapter that the absolute arrest of nutrition is followed by the complete cessation of all manifestations of vitality and function, constituting local or systemic death. Those conditions must now be considered in which the interference with nutrition, for the most part, falls short of absolute arrest, and in which, although vitality is impaired, death is only an occasional sequence. Such conditions are comprised under "Atrophy," and "Degeneration."

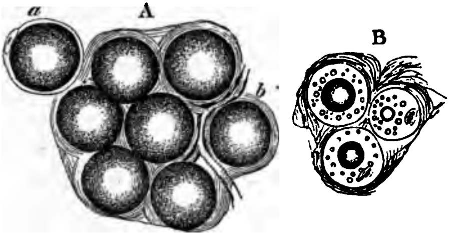
ATROPHY.

Atrophy is a diminution in the amount of a tissue, owing either to diminution in the *size*, or diminution in the *number*, of the histological elements of which it is composed. It is attended by loss of weight, and impairment of function.

When the elements are diminished in *size* only, it is called *Simple Atrophy;* when the *number* is diminished, it is called *Numerical Atrophy.* These two varieties are often associated, being different stages of the same process: *simple* atrophy may, however, exist without *numerical* atrophy, but *numerical* never exists without *simple.*

I. Simple Atrophy.—Simple diminution in the size of the elements of a tissue is by far the most common condition met with in atrophy. It is well exemplified by what takes place in ordinary emaciation, in which the fat gradually disappears from the subcutaneous adipose tissue. Adipose tissue is merely a connective tissue, the cells of which are distended with fat. When a person emaciates, the fat is gradually removed from the cells, so that they diminish in size, and the fat which completely filled the cell may be reduced to a few isolated drops: the cell-wall and nucleus at the same time often become distinctly visible (Fig. 2). Here there is no destruction of the cells, no diminution in their number, but simply the removal of some of their contents.

FIG. 2.



Adipose tissue. A. Normal. B. Atrophic, from a case of phthisis. *a.* a single fat-cell with cell-wall, nucleus, and drop of fat. × 300. (Virchow.)

This diminution in the size of the elements may take place in any tissue. The cells of all glandular organs may thus become atrophied, and so produce a diminution in the size of the whole organ; this is constantly met with in the liver, kidneys, mammary gland, spleen, testicles, lymphatic glands, and other parts. Muscular tissue in the same way atrophies by the diminution in the size of its primitive fasciculi: this is seen in the heart and in the voluntary muscles. In all these cases the elements remain almost unchanged; and hence all that is necessary for the restitution of the tissue is an increase in their nutritive activity, and the assimilation of more material.

II. NUMERICAL ATROPHY.—This is an advanced stage of the former process: the elements are not only diminished in size, but some of them have actually perished and ceased to exist as vital agents.

This destruction of histological elements which occurs both in atrophy and in degeneration—and is called by Virchow, *Necrobiosis*—must be distinguished from the death of circumscribed portions of tissue which constitutes gangrene and necrosis. The two processes resemble one another in so far as death is common to both of them. In *Necrobiosis*, however, the change is a molecular one; there is a gradual exhaustion of vital power, a molecular disintegration and destruction of elements, so that at the termination of the process all that remains is a granular débris, in which no trace of the former structure of the part can be discovered. The death and desquamation of the superficial layers of the epidermis is a well-known example of this molecular change. *Gangrene*, on the other hand, affects circumscribed tracts of tissue, and is the result of some sudden arrest of nutrition, as distinguished from the gradual exhaustion of vital power. Death is more suddenly induced, and a necrosed mass remains at the termination of the process in such a condition that the structure of the part can usually be recognised. Numerical atrophy is thus of much graver import than that in which the elements continue to exist as such. In it, restitution is only possible by the production of new elements, whereas in simple atrophy, repair can be effected without new formation.

Atrophy may be *general*—affecting to a greater or less extent all the organs and tissues of the body, or it may be *partial* and limited to particular parts. General atrophy is usually *simple*, and is rarely accompanied by destruction of elements. It affects in the first place the subcutaneous adipose tissue, then the adipose tissue in other situations, as that surrounding the viscera and [in the omentum, then the muscles and glandular organs, and lastly the nervous and osseous structures.

Although "atrophy" in its strict signification consists simply in a diminution in the size or number of the component elements of a tissue, it is rarely a perfectly simple process, but is usually associated with more or less *fatty degeneration*. This is owing to the fact that whenever the nutrition of a part is so much interfered with as to cause it to atrophy, it is very prone to undergo fatty changes; and it will be seen when speaking of "fatty degeneration," that this process owes its origin to the same causes as atrophy itself.

CAUSES.—In speaking of the causes of atrophy, it will be necessary to distinguish between those which act upon the tissues generally, and those which have merely a local influence.

General Atrophy may be caused by:—

1. *Deficient supply of Nutritive Material.*—Whatever interferes with the supply of nutritive material to the tissues will be followed by their atrophy. Deficient supply of food; obstruction to the passage of the food into the stomach or intestines, as in stricture of the œsophagus or pylorus; the mal-assimilation which results from the various conditions giving rise to dyspepsia; interference with the absorption of the chyle, from obstruction of the thoracic duct, or disease of the mesenteric glands constituting the so-called "tabes mesenterica;" may all in this manner be causes of general atrophy.

2. *Excessive Waste.*—All those conditions which are attended by the loss of large quantities of nutritive material, may be causes of general atrophy. Such conditions are furnished by continuous hæmorrhages, profuse

and long-continued suppuration such as occurs in caries and empyema, diarrhœa, and the excretion of large quantities of albumen or sugar as in Bright's disease or diabetes. The waste resulting from the increased tissue-change which accompanies acute febrile diseases, must also be included under this head.

4. *Impaired Nutritive Activity.*—This constitutes an important element in the production of the atrophy of old age,—*senile atrophy.* As life advances, the vitality of the elements gradually diminishes, their ability to separate nutritive material from the blood and to assimilate it for their own maintenance becomes less and less, and hence they gradually atrophy, and ultimately all manifestations of their vitality cease.

Although general atrophy may thus be referred to one of the foregoing causes, it is rarely a simple process, but usually depends upon the combined influence of two or more of them. The atrophy associated with pulmonary phthisis, for example, results partly from the loss of nutritive material in the profuse expectoration and diarrhœa, partly from the deficient supply consequent upon the interference with assimilation by the structural changes in the stomach and intestines which accompany it, and partly from the increased tissue-change. In senile atrophy, again, in addition to the general diminution of nutritive activity, there is frequently some condition of the digestive organs interfering with assimilation, which materially aids in producing the ultimate result. The atrophy which accompanies the acute febrile diseases is by no means a simple process, increased tissue-change, loss of appetite, and interference with assimilation being all essential parts of it.

Partial Atrophy may be caused by :—

1. *Imperfect supply of Blood.*—The effect of interfering with the supply of blood to a part will depend upon the extent of the interference. If it be entirely cut off the part

will die (See "Gangrene"), if merely diminished it will atrophy.

Diminished supply of arterial blood is a common cause of atrophy, and may be brought about in various ways. The nutrient vessels may be obstructed by pressure exercised upon them within or without the organ to which they are distributed. In cirrhosis of the liver, the increased growth of inter-lobular tissue by its pressure upon the capillaries causès atrophy of the secreting structures. In other cases the supply of blood is diminished by interference with the circulation at some distance from the part, as by the pressure of a tumour upon the artery leading to it. The atrophy of the proximal end of the shaft of a bone after fracture above the point of entrance of its nutrient artery, is due to the same cause.

The atrophy which results from pressure exercised directly upon the part itself, is probably also partly owing to the consequent interference with its nutritive supply. Atrophy of the sternum from the pressure of an aneurism, atrophy of the kidney from the pressure of retained secretion—as in stricture of the urethra, enlarged prostate, &c., and atrophy of the skull in chronic hydrocephalus, are well-known examples of these atrophies from pressure.

Mechanical congestion in the same way is not an uncommon cause of atrophy. The circulation is impeded, the blood is not returned normally by the veins, hence there is deficient arterial supply, and atrophy results.

2. *Diminished Functional Activity.*—This is the most common cause of atrophy, many examples of which are furnished both by physiological and pathological processes. After birth those parts which are no longer required to serve any purpose in the economy gradually atrophy and waste. The ductus arteriosus, the umbilical arteries and vein, the Wolffian bodies, and later—the thymus gland, all in this manner disappear. The invo-

lution of the uterus after delivery, the wasting of the spleen and lymphatic glands in advanced life, and of the lower jaw after the loss of the teeth, are other physiological examples of atrophy from this cause.

Muscles which from any cause have long remained inactive, atrophy. This is seen in the various forms of paralysis, especially in the so-called "essential paralysis" of children; also in limbs which have become incapacitated either on account of anchylosis, or of chronic diseases of the bones or joints.

After the establishment of an artificial anus, the lower part of the intestine atrophies, and becomes converted into a fibro-cellular cord.

Bones in the same manner atrophy from want of use. After the amputation of a limb, the cut end of the bone atrophies; and atrophy of the orbit follows extirpation of the eyeball.

Interference with the function of nerves is also followed by their atrophy: this is seen in the atrophy of the optic nerve, in some cases of blindness.

3. *Increased Functional Activity.*—This may occasionally be a cause of atrophy; much more commonly, however, it is a cause of hypertrophy. Some glands atrophy from excessive use, especially the testicle. The brain may also atrophy from over-work.

4. *Inflammation.*—This is a common cause of atrophy. The vitality of the tissue sometimes becomes so much impaired by the inflammatory process, that it consequently atrophies, degenerates, or dies. This will be considered when treating of "Inflammation."

5. *The Action of Special Substances.*—Certain substances administered internally appear to be capable of producing atrophy. Iodine, bromine, mercury, lead, and the alkalies, may be enumerated amongst the most important of these. Iodine and mercury exercise a special influence upon the lymphatic system, and bromine upon the organs of generation.

6. *Nervous Influence.*—Respecting the influence of the nervous system as a *direct* cause of atrophy, little is certainly known. That atrophy is a frequent sequence of changes in the nerve-trunks and nervous centres, there can be no doubt; but it is probably in many cases to be attributed to an *indirect* influence. The atrophy of muscles, for example, which have become paralysed from lesions in the brain or spinal cord, is often rather the result of the consequent interference with their function, than of any direct influence upon their nutrition. The rapid atrophy of muscles, however, which follows certain alterations in the nervous centres and injuries of the nerve-trunks, render it exceedingly probable that many nerves contain fibres which exercise a direct influence upon nutrition, and that nervous influence is not unfrequently a *direct* cause of atrophy (See "Introduction"). In some cases also, changes in the nervous system may cause atrophy by affecting the size of the blood-vessels, and so interfering with the supply of blood.

Physical Characters.—The estimation of atrophy is often a matter of considerable difficulty. The great criterion is, diminution in absolute weight. The weight of an organ, however, varies considerably in health; it varies with the weight of the body as a whole, and it may be less than natural from incomplete development. The same is true also of the muscular and osseous systems. An accumulation of blood and serosity in an organ may again increase its weight, and thus constitute a source of fallacy. This is often the case in organs which have been for some time mechanically congested, in which, although their size and weight may be increased, their tissue is considerably diminished in amount.

Organs which are atrophied are diminished not only in weight, but usually also in size. In most cases they contain less blood, they are dryer, firmer, and more fibrous in consistence than in health. Their functional powers are invariably diminished.

The whole of the textures of which an organ is composed may suffer; some, however, do so more than others. The fibrous constituents, instead of diminishing, may rather increase in amount. This is especially the case in senile atrophy: hence the firmness, toughness, and loss of elasticity so commonly met with in the atrophied parts. In glandular organs, the secreting cells are usually the first to show signs of atrophy; they become smaller, and are often finely granular, from the presence of molecular fat: the vessels and nerves also share in the wasting process. In the subcutaneous cellular tissue, the fat is gradually removed from the cells, which thus diminish in size. In muscles, the primitive fasciculi become smaller, and their transverse striæ gradually disappear; ultimately the whole of the contents of the sarcolemma may be entirely removed, and nothing remain but the connective tissue. This process is usually accompanied by more or less fatty degeneration of the muscular fibres, and in some cases by the development of fat between the fasciculi. (See "Fatty Infiltration of Muscle.")

Atrophy of bone is always attended by a diminution in weight, but not always by a diminution in size. The compact and cancellous tissue may gradually become absorbed, and the medullary canal diminish in size, the whole bone thus becoming smaller. This has been called *concentric atrophy*, and is met with especially in the long bones, in cases of long-standing anchylosis, dislocations, or paralysis. In other cases there is no diminution in the size of the bone, but merely a gradual conversion of compact into cancellous tissue: this, in contradistinction to the former variety, has been called *eccentric atrophy*, and is usually met with as a senile change.

DEGENERATION.

The "Degenerations" include a class of morbid processes which are characterized by an alteration in the *quality* of the tissues, and which, like atrophy, are attended by impairment of function, and often by annihilation of histological elements.

The alteration in the quality of the tissue results either from its direct metamorphosis into a new material, or from its infiltration with some substance which has been conveyed to it from without.

Atrophy and degeneration thus so far resemble one another, that in both processes nutrition is impaired and function interfered with. In atrophy, however, nutrition is simply altered in *quantity*, the waste of the tissue is in excess of the assimilation of new material, and consequently, there is a diminution in the amount of the tissue and an impairment of its functional powers. In degeneration, on the other hand, nutrition is altered in *quality*, a new substance exists in the tissues, which either originates in the tissue itself, or infiltrates it from without; this is attended by impairment of the vitality and functions of the elements of which the tissue is composed, resulting either from the presence of the new material, or dependent upon the same conditions as those which give rise to its formation.

CAUSES.—Of the causes of the Degenerations as a class, but little can be said, the various forms depending for the most part upon different conditions. These will be described under their respective heads. Fatty and calcareous degeneration have, however, many points in common, and they are both intimately connected with the atrophic changes; atrophy, fatty, and calcareous degeneration are indeed frequently different stages of the same process, and the causes of these two forms of degeneration will thus be seen to be very similar to those already enumerated as causes of atrophy.

The Degenerations may be divided into two classes—the *Metamorphoses* and the *Infiltrations*.

1. THE METAMORPHOSES.—These are characterized by the direct metamorphosis of the albuminoid constituents of the tissues into a new material. This is usually followed by the destruction of the histological elements and the softening of the intercellular substance, so that ultimately all trace of structure may be lost, and function be completely arrested. The Metamorphoses include Fatty, Mucoid, and Colloid Degeneration.

2. THE INFILTRATIONS.—These differ from the Metamorphoses inasmuch as the new material which exists in the tissues is not derived from their albuminoid constituents, but is deposited in them from the blood: there is an infiltration and deposition of a new substance. This is rarely followed by destruction of the histological elements, or by softening of the intercellular substance; hence the anatomical characters of the tissue are much less altered than in the Metamorphoses, and function is much less interfered with. The Infiltrations include Fatty, Amyloid, Calcareous, and Pigmentary Infiltration.

CHAPTER IV.

THE METAMORPHOSES.

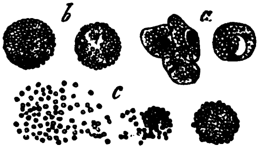
FATTY DEGENERATION.

This is the most important of the degenerative processes, not only on account of its extreme frequency, but also from the deleterious effect it produces in those tissues which are affected by it.

The process consists in the transformation of the albuminoid constituents of the tissues into fat, the cells being the parts which are most frequently affected. This fat makes its appearance as minute granules and molecules within the cells, usually first in the protoplasm, and subsequently in the nucleus. The granules—which are characterized by their dark colour, sharp contour, strong refractive power, and solubility in ether—gradually increase in number, until the whole of the protoplasm has undergone the transformation. As they increase some of them may coalesce, and so form distinct drops of fat: this, however, is not common, the fat usually remaining to the last in a granular form. As the process proceeds the cells undergo an increase in size and become more globular in shape. Ultimately the nucleus becomes involved, the cell-wall, when this exists, is destroyed, and the cell is thus transformed into a mass of granular fat (Fig. 3).

These granules of fat may remain in a coherent form for some time after the cell-wall and nucleus are destroyed; they then constitute the so-called "inflammatory" or "exudation corpuscles," or "corpuscles of Gluge," which are so common in chronic cerebral softening, and in other forms of fatty degeneration (Fig. 3 *b*). Ultimately the corpuscles break up, the albuminous matter between the granules of fat liquefies, and the fat becomes distributed in the tissue (Fig. 3 *c*).

FIG. 3.



Fatty degeneration of epithelium. a. Cells containing molecules of fat. *b.* Granular corpuscles; in one nucleus is still visible. *c.* Disintegration of corpuscles. (Rindfleisch.)

Types of this pathological condition are furnished by many well-known physiological ones, one of the most characteristic of which is perhaps the secretion of milk. The mammary gland is a large racemose gland, consisting of innumerable groups of lobules lined with epithelial cells. The secretion of milk takes place in the following manner:—The cells lining the lobules of the gland multiply abundantly, and the new cells as they are produced gradually become converted into fat; the cell breaks up, and the fatty matters in a more or less coherent form constitute the milk-corpuscles. At the commencement of the process the granules of fat cohere and form colostrum-corpuscles; but as the secretion becomes fully established, and the multiplication and disintegration of the cells takes place more rapidly, the fatty molecules become at once distributed in the liquid in which they are suspended, giving to the secretion its characteristic white colour. The milk-corpuscles thus formed are replaced by the continuous formation of new cells from below, which in their turn undergo fatty degeneration, and in this manner a continuous formation and destruction of cells takes place.

Other examples of fatty degeneration are afforded by the formation of the sebaceous matter of the skin, the cerumen of the ears, and the corpus luteum in the ovary; all of which take place in the same way by the fatty metamorphosis and destruction of newly formed cells.

The immediate effect of fatty degeneration is to produce more or less softening of the affected part, the cellular elements are completely destroyed, the intercellular substance also undergoes fatty changes, and thus all trace of the original structure may be ultimately lost. This destruction of the cells is the essential feature of the change, and distinguishes it from fatty *infiltration*, in which the cells within which the fat accumulates remain intact (see " Fatty Infiltration").

If large tracts of tissue are affected, the change is readily recognisable by the naked eye, by the diminution in consistence and elasticity which are produced, and in many cases also by the opaque yellowish-white colour. If, however, the change is limited to minute and isolated portions of the tissue, its existence can only be discovered with the aid of the microscope.

The fatty particles into which the cells have been transformed, under favourable circumstances are readily absorbed. This is seen in the fatty degeneration and absorption of inflammatory products, as in croupous pneumonia. In order for such absorption to take place, it is necessary that the tissue should be freely supplied with blood-vessels. If this is not the case, the degenerated products are liable to undergo certain changes whereby they become converted into a pultaceous crumbling material somewhat resembling cheese:—this is known as *caseation*.

CASEATION.—This is a modification of the degenerative process in which the fatty products gradually dry up into a yellowish friable material, which has been compared to soft cheese. This change appears to be owing to a natural dryness of the degenerated tissue, resulting from deficient vascular supply. It is most frequent in parts which contain but few vessels, or in those in which these become obliterated by some new growth. Growths composed of closely-crowded cells—as tubercle, epithelial accumulations within the pulmonary lobules, growths in the lymphatic glands, in the brain, and in the osseous structures, are the most liable to become caseous.

The process consists in a gradual drying up of the degenerated elements; the fluids are absorbed, the cells —which are many of them incompletely degenerated— shrivel and atrophy, the fat undergoes partial saponification, cholesterine forms, and the tissue thus becomes converted into a soft, yellowish-white, cheesy substance, composed of atrophied cells, fatty débris, and cholesterine crystals. This material may gradually dry up more and more, and ultimately become encapsuled by a layer of fibrous tissue.

These cheesy matters are constantly met with, especially in the lungs, and considerable confusion has arisen as to their nature and origin in this situation. This has proceeded from its having been formerly the custom to look upon all cheesy masses as essentially tubercular. Tubercle, it is true, often undergoes, to a greater or less extent, fatty degeneration; and it may thus, like all other structures which have undergone this process, become converted into a yellow cheesy substance; but it is by no means true that all cheesy masses are tubercular. Thus the pathological significance of these cheesy masses is much less limited than was formerly supposed, and is indeed almost coextensive with that of fatty degeneration itself. In whatever situation they are met with, they indicate merely that the histological elements have undergone this fatty metamorphosis, and under no circumstances are they in themselves evidence of any one particular form of morbid growth.

The caseous mass may subsequently become calcified, or undergo a process of softening and liquefaction.

Calcification.—This is an advanced stage of the preceding process. It most frequently occurs in those cases in which the caseous mass is completely enclosed and isolated from the external air, as when in the lymphatic glands, in bone, or when encapsuled in the lungs. The mass becomes infiltrated with calcareous particles, and is thus converted into a calcareous concretion (see "Calcareous Degeneration").

Softening.—This process consists in a liquefaction of the caseous substance, which is probably owing to some chemical change in its constituents. It commonly occurs in parts which come into contact with the external air, especially in those situated in the intestine, in the bronchial mucous membrane, and in the pulmonary lobules. The caseous mass liquefies, and is converted into a thin puriform fluid, containing curd-like cheesy matter, which to the naked eye looks much like pus, but under the microscope is seen to consist simply of granular débris, fat, and cholesterine crystals. This, if not discharged, may, like the caseous masses, ultimately dry up and become calcified.

Causes.—All those conditions which tend to interfere with nutrition, and have been already enumerated as causes of atrophy, predispose to this fatty change. It may indeed be looked upon as an advanced stage of the atrophic process.

Diminished supply of blood is a common cause of fatty degeneration. This is seen in chronic cerebral softening, which is intimately connected with the interference with the circulation consequent upon disease of the cerebral blood-vessels. In the heart, again, this form of degeneration is not an infrequent concomitant of disease of the coronary arteries. The circulation may also be interfered with by pressure from without, as by the growth of adipose tissue between the fasciculi of muscle, in which case the muscle undergoes fatty degeneration. The degeneration of the hepatic cells in cirrhosis of the liver is due to the same cause. Inflammation, again, is a most potent cause of this degeneration, as is exemplified by its effect upon nearly every organ and tissue. This result is owing partly to the disturbance of the circulation, and partly to the rapid production of new elements. The vitality of a part may become impaired by its rapid growth, the production of new tissue being out of proportion to the vascular supply. This explains the degeneration and softening so liable to occur in all rapidly growing new formations; the softening of the central portions of cancerous and sarcomatous tumours, &c., being very familiar examples. Lastly, the impaired nutritive activity of the tissues, which results from old age, is a most common cause of their fatty degeneration. All tissues may undergo, more or less, this senile change, but it is especially marked in those in which there is normally a somewhat imperfect arterial supply, as cartilage and the cornea ("arcus senilis").

It will thus be seen that fatty degeneration is a common termination of many morbid processes which tend to impair the vitality of the parts affected by them; and that this impairment of vitality is the invariable antecedent of the fatty change,—the change itself merely indicating that, from some cause or other, the vitality has been diminished. The pathological significance of fatty degeneration thus becomes in many cases a question of considerable difficulty, it being often impossible, from an examination of the degenerated parts alone, to decide upon the nature of the antecedent condition. In many cases of fatty degeneration of the kidney, for example, in which the cells lining the tubuli uriniferi are destroyed and the tubes themselves are filled with the fatty débris, it is often impossible to say, from an examination of the tubes alone, whether the fatty change is secondary or not to an inflammatory process. It is only when an investigation of the first stages of the process is practicable that the discovery of its real nature becomes possible.

With regard to the source of the fat, it is, as already stated, derived directly from the tissue itself, and is not infiltrated from without. The exact nature of the change appears at present to be somewhat uncertain. It is most probable, however, that it is simply a liberation of the fat which is naturally combined with the albuminoid constituents of the tissues, and is not a direct conversion of nitrogenous into fatty matter. Whether this be so or no, the formation of the fat is undoubtedly the result of impaired nutrition, and as Dr. Quain has shown, it may take place in tissues after death, from the spontaneous decomposition of their nitrogenous constituents.

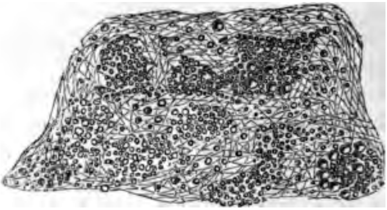
FATTY DEGENERATION OF ARTERIES.

Fatty degeneration of arteries may be a primary or secondary affection. As a secondary process it is met with in Atheroma, in which the fatty change is preceded by an inflammatory cellular infiltration of the subendothelial connective tissue (see "Atheroma").

Primary fatty degeneration is a passive process, not being preceded by any increased nutritive activity of the parts affected by it. It may affect both the internal and middle coats of the artery, but it is most common in the former situation. The change usually commences in the endothelium and the connective tissue cells in the most internal layers of the inner coat, small groups of cells becoming affected in various parts of the vessel; and it may gradually extend from within outwards, the intercellular substance softening, until in exceptional cases, the whole thickness of the intima is destroyed. (Fig. 4.)

In the earlier stages of the process, the condition is recognised by the existence of small irregular-shaped

FIG. 4.



Fatty Degeneration of the Internal Coat of the Aorta. Minute yellowish-white patches scattered over the lining membrane of the vessel. A very thin layer peeled off and × 200, showing the groups of fat-molecules, and the distribution of fat in the intima.

patches of an opaque yellowish-white colour, projecting very slightly above the surface of the intima. These, which are so constantly met with on the lining membrane of the aorta, may at first be mistaken for Atheroma: they are in most cases, however, readily distinguishable by their superficiality, and by the facility with which they can be stripped off from the subjacent layers, which present a natural appearance. In Atheroma on the other hand—which affects the deeper structures,—if the superficial layer be removed, the opacity and thickening are seen to exist beneath it. In many cases the change is limited entirely to the endothelial lining of the vessel; the more the subjacent tissues are involved, the greater is the irregularity in the shape of the patches, and the less readily can they be separated with the forceps. The opaque patches ultimately break down, the cells are destroyed, the intercellular substance softens, and the granular débris is carried away by the circulation, leaving small, irregular, superficial erosions upon the lining membrane of the vessel. These erosions are not ulcers in the true sense of that term, not being the result of an active process. They resemble the superficial erosions so common upon the mucous membrane of the stomach, as described by Dr. Wilson Fox.

Simple fatty degeneration may occur in any of the arteries, but it is in the smaller ones that its injurious influence is most marked. Here, by diminishing the elasticity and contractility of the vessels, it causes degenerative changes in the parts which they supply, and often leads to rupture. This is exemplified by many cases of chronic cerebral softening, cerebral hæmorrhage, and fatty degeneration of the heart, all of which are frequently due to this disease of the nutrient vessels. In the larger arteries, as the aorta—where it is exceedingly common—it is of less importance, the inflammatory process, atheroma, having here a far more deleterious effect.

The capillaries may also be the seat of this fatty change; the endothelial cells being destroyed in the process, and the walls so much damaged, that rupture is often the ultimate result. This is very common in the smallest cerebral blood-vessels, where it is a frequent cause of cerebral hæmorrhage.

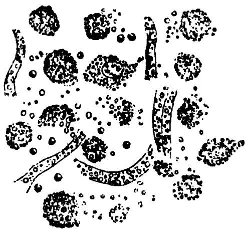
Passive fatty degeneration of arteries is in most cases a senile change; it is an expression of that general impairment of vitality which exists in advanced life, and is usually associated with similar changes in other parts. When, however, it is limited to the largest arteries, it is often met with in early life and in persons who are otherwise perfectly healthy.

FATTY DEGENERATION OF THE BRAIN.

Fatty degeneration of the brain is met with in all those morbid conditions comprised under the common term of "Cerebral Softenings." Whatever impairs the vitality of the cerebral substance will tend to produce fatty degeneration, and hence, softening. The portions of the brain which are the seat of this change may be merely rather softer than the surrounding healthy tissue —breaking down more readily under a stream of water which is allowed to fall upon them—or they may be completely diffluent. They are never distinctly circumscribed, but pass by insensible gradations into the neighbouring tissue.

Under the microscope the change is seen to consist in a disintegration of the nerve-tissue. The white substance of the fibres first coagulates, then breaks up into large masses, and these subsequently undergo fatty metamorphosis. The cells of the neuroglia and the small blood-vessels are also involved in the fatty change. The tissue is thus converted into broken-down fibres, a large amount of molecular fat, and numerous large granular corpuscles, the so-called "exudation corpuscles" or "compound inflammatory globules of Gluge." (Fig. 5.) These corpuscles were formerly looked upon in all cases as the result of inflammation, hence their name; they are, how-

FIG. 5.



Chronic White Softening of the Brain. Showing the granular corpuscles, broken-down nerve-fibres, and fat granules, of which the softened substance is composed. One or two nucleated cells (probably nerve-cells) are also visible. × 350.

ever, simply conglomerations of fat granules formed by the degeneration of the cellular elements. (See "Fatty Degeneration," Fig. 3.) The cells from which they originate are, according to Virchow and Robin, the cells of the neuroglia—the connective tissue of the brain:—these cells share in the fatty change, and in doing so, appear to undergo considerable enlargement before they are destroyed and the fatty matter breaks up. They vary in size from $\frac{1}{500}$ to $\frac{1}{2000}$ inch in diameter, the average being $\frac{1}{1000}$. When the softening affects the grey matter the nerve-cells also contain molecular fat. The small arteries and capillaries running through the softened part are many of them filled with fat granules and granular cells: these latter probably originate in the white blood-corpuscles which have accumulated in the part and undergone fatty changes. Molecular fat and the large granular corpuscles will also be seen adhering to the external surface of the vessels; and here care is required to distinguish these from fatty degeneration of the vessels themselves, to which the cerebral softening is so frequently due. As the process proceeds the cerebral substance is completely destroyed and all traces of nerve-structure is ultimately lost.

The colour of the softened portion varies considerably. It may resemble that of the surrounding healthy tissue; in other cases it is altered to a yellowish or deep red tint. According to these variations in colour, cerebral softenings have been classified into *white*, *yellow*, and *red*. The colour depends in great measure upon the amount of blood contained in the part, and on this account is important, as indicating the manner in which the softening has been brought about.

White Softening.—This is, in the great majority of cases, a chronic condition, dependent upon disease of the capillaries and small arteries, which interferes with the circulation, and thus impairs the vitality of the part. There is no hyperæmia, and the colour either resembles that of healthy brain-tissue, or is an opaque dirty white. White softening is sometimes acute, in which case it is usually due to the sudden obstruction of the circulation by the impaction of an embolus in one of the larger arteries. (See "Embolism in the Brain").

Yellow Softening.—This is, in most cases, simply a variety of the former process, in which, from the fine state of division and close aggregation of the fatty particles, a dead yellowish-white colour is imparted to the softened tissue. This colour is probably often partly owing to the presence of altered blood pigments, the result of some previous slight extravasation. The pigment may sometimes be seen as fine dark granules, scattered through the cells of the neuroglia and the nerve-cells of the grey matter, where at first sight they look like fatty particles; they are distinguished, however, by their dark black colour. Yellow softening may also result from embolism and hæmorrhage.

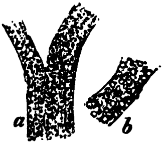
Red Softening.—This is commonly an acute affection, most frequently dependent upon vascular obstruction, either from embolism or thrombosis. There is intense collateral hyperæmia, rupture of capillaries, and extravasation of blood; the softened tissue is consequently of a deep red colour:—this will be described in the chapter on "Embolism." Red softening is also sometimes associated with the chronic white variety, some of the diseased vessels giving way, and thus extravasation of blood taking place into the already softened tissue. Lastly, red softening may be inflammatory (see "Inflammation of the Brain").

FATTY DEGENERATION OF MUSCLE.

Both striated and non-striated muscle may be the seat of fatty degeneration. In the latter, the muscular cells which constitute the involuntary muscular fibres, are the seat of the change; they become filled with fat granules and are ultimately destroyed. This condition is frequently met with in the middle coat of arteries which are undergoing fatty degeneration.

In striated muscle—both in the voluntary and in the involuntary of the heart—the fibres themselves are the seat of the morbid process, which consists in the conversion of the albuminoid matter of which the fibre is composed into fat. The earliest stage of the affection is characterized by an indistinctness in the transverse markings of the fibres, which in many parts become studded with minute particles of fat. (Fig. 6.) These gradually increase in number and size, and are usually distributed somewhat irregularly within the sarcolemma. In some parts single rows of granules are found running along the length of the fibre; in others, they are grouped around the nuclei or arranged in transverse lines corresponding with the striæ of the muscle. The fibres become extremely friable, and are readily broken up into short fragments. As the process proceeds the transverse markings entirely disappear, and nothing but molecular fat and oil globules are seen within the sarcolemma. The sarcolemma itself may ultimately be destroyed, and nothing remain of the original fibre but the fatty débris into which its albuminoid constituents have been converted. This is true fatty degeneration of muscle; in it the muscular elements are destroyed, and it thus differs essentially from fatty *infiltration*, in which there is simply a development of fat between the fasciculi, the fasciculi themselves not being primarily affected (see "Fatty Infiltration of Muscle").

FIG. 6.



Fatty Degeneration of Muscular Fibres of Heart. *a.* Earlier stage. *b.* more advanced. × 400.

FATTY DEGENERATION OF THE HEART.

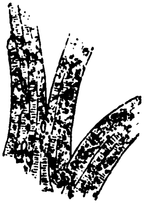
It is in the heart that fatty degeneration of muscle is most frequently met with, and here it assumes a most important aspect from the deleterious influence which it exercises upon the motor power of the organ. The muscular substance may be affected throughout, or, as is more frequently the case, the degeneration may be confined to certain portions of it. It is more common in some situations than in others. The order of frequency with which it occurs in different parts is, according to Dr. Quain, firstly, the left ventricle; secondly, the right ventricle; thirdly, the right auricle; and fourthly, the left auricle.

The wider the extent of tissue that is affected, the less advanced, as a rule, is the degree of the degeneration. It is in those cases in which small tracts of tissue are involved, that the process is met with in its most advanced stage.

The consistence of the degenerated part is always diminished, and its colour altered. When the change is slight, and more or less general, the muscle is somewhat softer and more flabby than natural; it is more friable, and often breaks with a soft granular fracture. The colour is uniformly rather paler, and more opaque than that of healthy cardiac tissue. Under the microscope the muscular fibres are seen to have lost their striated appearance, and to contain minute granules of fat (Fig. 6 *a*); there are, however, no large molecules or oil globules, and the sarcolemma is not destroyed. This diffuse form of degeneration sometimes occurs in the course of acute febrile diseases, and it may also be a part of general marasmus.

More frequent than this diffuse and slight degree of degeneration affecting the whole or the greater part of the organ, is a condition in which, although perhaps the change may be more or less general, it is much more advanced in some parts than in others. In such cases the heart presents a mottled appearance; numerous opaque, pale yellowish or brownish patches are seen irregularly distributed throughout its substance. These patches vary considerably in size and form; they are met with especially in the papillary muscles, the columnæ carneæ, and in the layers of fibres immediately beneath the endocardium: they may also occur beneath the pericardium, and in the deeper portions of the organ. They correspond with the most degenerated portions of the tissue. They are soft and flabby, and have a rotten consistence, tearing readily under the finger. Under the microscope, the fibres are seen to be in an advanced stage of fatty degeneration; their sarcolemma contains large molecules of fat and oil globules, which in many parts have escaped and lie free amongst the surrounding less degenerated tissue. (Fig. 6 *b*.) These smaller tracts of degenerated tissue in which the change is more advanced, often result from localized obstructions to the circulation consequent upon disease of the coronary arteries. They are also met with close beneath the endocardium in some cases of extensive dilatation and hypertrophy. Lastly, the peripheral layers of muscular tissue frequently undergo extensive fatty degeneration as the result of pericarditis.

FIG. 7.



Brown Atrophy of the Heart. Showing the granules of pigment and the atrophy of the fibres. The latter have in some parts undergone slight fatty metamorphosis. × 400.

BROWN ATROPHY OF THE HEART.

Closely allied to, and frequently associated with fatty degeneration of the heart, is the condition known as brown atrophy. This consists in a gradual atrophy of the muscular fibres, together with the formation of granules of blackish or brownish-yellow pigment. These granules of pigment are either *grouped in clusters* around the nuclei, or more generally distributed within the fibre. The fibres are frequently, at the same time, the seat of more or less fatty degeneration. (Fig. 7.)

Brown atrophy of the heart usually occurs as a senile change, or as a part of general marasmus from other causes. It is also met with in some cases of cardiac hypertrophy. It is more chronic in its course than simple fatty degeneration, and its recognition is in most cases impossible without the aid of the microscope.

CHAPTER V.

MUCOID AND COLLOID DEGENERATION.

UNDER this head is included a class of morbid changes which are characterized by a peculiar softening of the tissues. Colloid and mucoid degeneration have frequently been described under the common term of "colloid softenings," but—although they are very closely allied and frequently associated—they appear to constitute two distinct processes; the former affecting especially the cells, the latter the intercellular substance.

MUCOID DEGENERATION.—This consists in a liquefaction of the tissues and an alteration in their chemical composition, owing to which they yield *mucin*, and become converted into a material of a soft, mucilaginous, jelly-like consistence. This is the condition of nearly all tissues in their immature or fœtal state: the connective tissues in the fœtus consist almost entirely of this soft mucin-yielding substance. Some tissues retain these characters after birth. The umbilical cord, and the vitreous humour of the eye, are both composed of this substance.

The change affects especially the intercellular substance, much less frequently the cellular elements. The intercellular substance of the connective tissues in their fully developed state consists of gelatin and chondrin, and the mucoid change is thus a reversion of this substance to its fœtal condition. As to the manner in which this takes place, nothing is known. It does not appear to be associated with any known general state, or with any previous change in the tissues in which it occurs. It probably depends upon some alteration in the vital performances of the cells, upon which the intercellular substance depends for its existence.

Mucin is closely allied to albumen, more so than to either gelatin or chondrin: it differs from it in not containing sulphur. Like albumen, it is only met with in alkaline fluids—being held in solution by the free alkali—from which it is precipitated by dilute acetic acid. It differs from albumen in being soluble in an excess of the acid, and also in not being precipitated by boiling, by tannin, or by bichloride of mercury: its behaviour with these two reagents will also distinguish it from gelatin and chondrin, which are both precipitated by them.

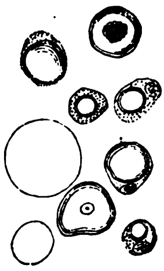
The mucoid change is by no means a common one. It is most frequently met with in cartilage, especially in the inter-vertebral and costal cartilages of old people; also in serous membranes, in the connective tissue of the choroid plexus and lateral ventricles, in bone, and in many of the new formations. Wherever it occurs it produces softening of the affected parts; which are transformed into a homogeneous, colourless material, of a soft mucilaginous jelly-like consistence. If the change is limited to isolated portions of the tissue, the softened parts surrounded by those which are unaltered, present the appearance of cysts. These cyst-like formations containing mucoid substance are not uncommonly met with in the costal cartilages, the choroid plexus, and in new growths.

The cells themselves appear in the majority of cases not to undergo the mucoid change. They are frequently, however, the seat of fatty metamorphosis; and they may also proliferate, as in mucoid new formations.

COLLOID DEGENERATION.—This differs from the former, *inasmuch* as it is the *cells* which are especially involved in *the process.*

The change consists in the metamorphosis of the albuminoid constituents of the cells into a substance known as *colloid* material. Colloid closely resembles mucous substance, but it differs from it chemically, in containing sulphur, and in not being precipitated by acetic acid. It is a colourless, transparent, glistening material of the consistence of jelly or half-set glue. It makes its appearance within the cells, as small lumps, which gradually increase in size, pushing the nucleus to one side, until they completely fill the cell (Fig. 8). The cells are thus destroyed, and converted into colloid masses. The small colloid masses subsequently swell up, coalesce, and so form larger masses of firm, transparent, yellowish, jelly-like material, which are readily recognised by the naked eye.

FIG. 8.



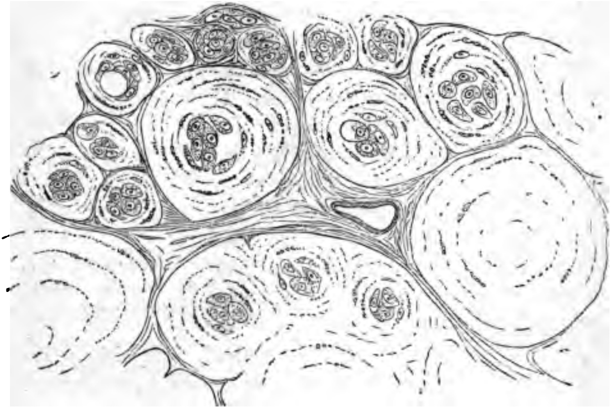
Colloid Cells, from a colloid cancer. (Rindfleisch.)

As the colloid matter increases and the cells are destroyed, the intercellular substance atrophies or softens, and in this way cyst-like cavities are formed within which is contained the gelatinous substance. Here it may subsequently undergo a process of liquefaction (Fig. 9).

The colloid change is most common in enlargements of the thyroid gland, in the lymphatic glands, and especially in many of their new formations. (See "Colloid Cancer.") Its causes and nature are as obscure as those of the allied mucoid softening.

It is when occurring in new formations that these two forms of degeneration assume their most important aspects. Many varieties of tumours may originate as mucoid or colloid growths, or may subsequently undergo these morbid *transformations*. The mucous tumours, *(myxomata,) which* resemble in structure the umbilical cord, consist entirely of a gelatinous mucus-yielding substance. The sarcomata, lipomata, enchondromata, and the cancers, may also become the seats of these forms of softening.

FIG. 9.



Colloid Cancer, showing cyst-like cavities filled with the colloid substance. × 300. (Rindfleisch.)

Such growths have frequently been described as gelatiniform or colloid *cancers*, this term having been applied to them without any regard to their structure or real nature. Cancers, it is true, may either originate as mucoid or colloid growths, or may become so after their development is completed (see "Colloid Cancer"); but it is by no means true that all tumours possessing these soft gelatiniform characters are cancers. The terms "mucoid" or "colloid" applied to a new growth, merely imply certain physical and chemical characters, and convey no information as to its real nature.

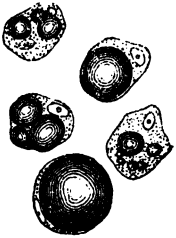
CHAPTER VI.

THE INFILTRATIONS.

FATTY INFILTRATION.

Fatty Infiltration—which is often described as "fatty degeneration"—consists in the infiltration of the tissues with fat, which is deposited in them from the blood. The fat is deposited within the cells, where it occurs as distinct drops; these may gradually accumulate and run together, displacing and obscuring the nucleus and protoplasm, until the cell is completely filled and distended with oil. (Fig. 10.) The vitality and functious of the cells are but little impaired by the accumulation, and the protoplasm—although rendered almost invisible when this is excessive—remains unaltered. This process therefore differs essentially from fatty degeneration, in which the fat is derived from a metamorphosis of the protoplasm itself, occurs in a granular form, and in which the cells themselves ultimately perish. (See Fig. 3). In fatty infiltration, the cells within which the fat accumulates not being destroyed, the *removal of the fat is all* that is necessary to *restore them to their original* condition.

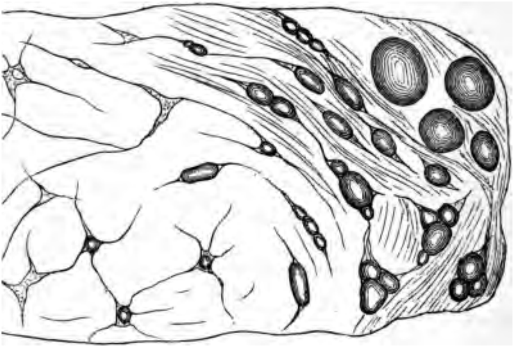
Fig. 10.



Liver Cells in various stages of Fatty Infiltration. × 300 (Rindfleisch).

Fatty infiltration occurs as a physiological process in the growth of adipose tissue. Adipose tissue bears a close resemblance to common connective tissue; it is connective tissue, containing numerous cells which are distended with fat. The growth of adipose tissue thus consists simply in the infiltration of more of these cells with fat. If this be excessive it constitutes obesity. (Fig. 11.)

FIG. 11.



Fatty Infiltration of Connective Tissue. Showing the accumulation of fat within the cells. × 300. (Rindfleisch.)

The temporary accumulation of fat in the intestinal villi and liver during the digestion of an aliment rich in fatty substances, is another example of physiological infiltration. This will be described when speaking of the "fatty liver."

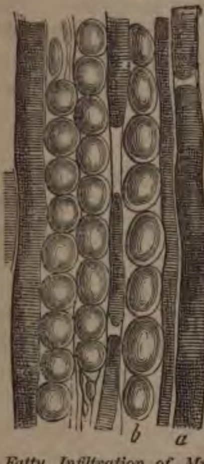
As a pathological process, fatty infiltration occurs either when the blood contains an abnormal quantity of fat, or when, owing to some change in a particular tissue, the fat normally contained in the blood tends to become deposited in it. The latter is seen in the fatty infiltration of paralysed muscles. (See "Fatty Infiltration of Muscle.") An absolute increase in the amount of fat in the blood is in many cases the result of excessive supply of nutriment, or to this combined with diminished waste. Such conditions obtain in people who live freely and take but little exercise. There appears to be in some a special predisposition to become fat. In other cases, the excess of fat in the blood is owing to its absorption from some particular tissue, subsequently to which it becomes deposited in another:—this is seen in the fatty infiltration of the liver, which is associated with the general emaciation of pulmonary phthisis and other similar conditions. (See "Fatty Infiltration of the Liver.") Why the deposition should take place in certain tissues, and the fat be removed from some and deposited in others, is not known.

FATTY INFILTRATION OF MUSCLE.

In muscle, fatty infiltration is frequently met with as a morbid process. The cells in the connective tissue which surrounds the fasciculi of the muscle become filled with fat; and this development of fat between the primitive muscular fasciculi has often been included under the common term of "fatty degeneration" of muscle. The process, however, differs essentially from true degeneration, in which the fat originates *within* the fasciculi and the fasciculus itself ultimately perishes; whereas in the condition now under consideration, there is a deposition of fat *between* the fasciculi, which remain—during the early stages at all events—unaffected. The interstitial fat varies in amount. In some cases single rows of fat cells alternate with rows of muscular fasciculi, at other times the accumulation is less regular, more existing between some fibres than between others; in all cases, however, the muscular elements may be discovered lying amongst the fat. (Fig. 12.) If the latter is very considerable in amount, the muscle may appear to the naked eye to be entirely converted into fat; but the microscope will always reveal the muscular structure in which it is embedded.

This condition is frequently met with in animals which have been fattened, the fat not only increasing in the usual situations, but also accumulating between the fasciculi of the muscles. In muscles also which from any cause have for some time been incapacitated, this interstitial growth is extremely liable to occur; ex. gr. in the extensors of the wrist-joint in cases of lead-poisoning, and in long-standing paralyses from lesions in the brain or cord, also in muscles which have been rendered useless by anchylosis of a joint. In progressive muscular atrophy, as Virchow has shown, the affected muscles exhibit this change, together with true fatty degeneration.

FIG. 12.



Fatty Infiltration of Muscle. *a.* Atrophied muscular fibres. *b.* Interstitial fat-cells. × 300. (Rindfleisch.)

In the *heart*, fatty infiltration is not unfrequently met with; and here it is especially important to distinguish it from the much more grave condition in which the fibres themselves are primarily affected. In health, there is a varying amount of fat covering the surface of the heart beneath the visceral layer of the pericardium, which is always most abundant in the grooves between the auricles and ventricles, where it surrounds the blood-vessels. This may increase so as to completely envelope the organ, and at the same time gradually insinuate itself between the muscular fibres, so that to the naked eye all appearance of muscular structure may be lost, the walls looking like a mass of fat. In hearts less affected, striæ of fat will be seen lying amongst the muscle. The fat is always most abundant near the surface, the muscular structure becoming more evident towards the endocardium.

The immediate effect of the interstitial growth is to displace and compress the muscular fibres between which it insinuates itself, and in doing so it diminishes the contractile power of the muscle: this is especially the case when occurring in the heart. The pressure, however, which it exercises upon the fibres and the accompanying blood-vessels, ultimately causes in the former atrophic and degenerative changes. Thus the fasciculi gradually atrophy, the transverse striation becomes indistinct and is replaced by molecular fat; in fine, true degeneration of the muscle is established. These two processes, indeed, not uncommonly go hand in hand together, the interstitial infiltration inducing the intrastitial degeneration.

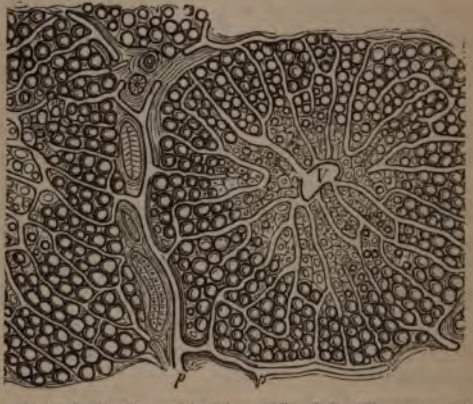
FATTY INFILTRATION OF THE LIVER.

It is in the liver that fatty infiltration assumes its most important aspect, and in this organ it is exceedingly frequent, constituting what is commonly known as the "fatty liver." It must be carefully distinguished from true fatty degeneration, in which the nutrition of the hepatic cells becomes impaired, and they consequently undergo retrogressive metamorphosis. The latter occurs in many structural changes of the liver, as cirrhosis, amyloid degeneration, &c., and is quite distinct from fatty infiltration.

The hepatic cells always contain a small quantity of fat, which is temporarily increased after the ingestion of fatty substances. It will be well to describe this physiological infiltration before proceeding to the morbid process.

The ingestion of an aliment rich in fatty substances is followed by a temporary excess of fat in the blood, and by the deposition and temporary accumulation of a portion of this within the hepatic cells. This fat is first deposited in the cells which are in immediate contact with the capillaries of the portal vein, and thus is produced an excess of fat in the cells at the circumference of the hepatic lobules. This gradually passes from the cells at the circumference to those in the interior, whence it is ultimately conveyed into the circulation. This process goes on until the excess of fat is removed from the blood, when the hepatic cells again acquire their former character. There is thus a transitory accumulation of fat within the hepatic cells which is gradually removed, the vitality of the cells not being thereby impaired.

FIG. 13.



Fatty Infiltration of the Liver. (*Somewhat diagrammatic.*) Showing the accumulation of fat in the external zone of the lobules. *V.* Hepatic vein. *p.* Interlobular portal vessels. (Rindfleisch.)

Precisely similar to the above is the morbid process. The morbidly fatty liver is one which contains an abnormal quantity of fat. This may result either from an excessive deposition from the blood, or from some interference with the removal of the temporary physiological accumulations. The fat being deposited from the blood in the portal capillaries, the increase is first observable in the external zone of the hepatic lobules. (Fig. 13.) It accumulates here within the cells as minute globules, which as they increase coalesce and form large drops of fat: these may ultimately completely fill and distend the cells, which at the same time become larger and more globular in shape. (See Fig. 10.) As the process proceeds, the accumulation advances from the periphery towards the centre of the lobule, until ultimately its whole mass may be involved, and the cells universally become distended with fat. The vitality of the cells is not materially impaired by the infiltration; they continue to perform their functions, as is shown by the presence of bile in the stools and in the gall-bladder.

The fatty liver is somewhat increased in size, in advanced stages often considerably so. The surface is smooth, the edges are thickened and rounded, the specific gravity is diminished, although the absolute weight may be increased. If the infiltration be slight, involving merely the portal zone of the lobules, the cut surface will present a mottled appearance, the external fatty zone being of an opaque yellowish-white colour, whilst the central portion remains unaltered, or is perhaps somewhat hyperæmic. The more extensive the infiltration the larger is the pale zone, and ultimately, when the whole lobule is involved, there may be left in the centre merely a reddish-brown point, which corresponds with the commencement of the hepatic vein; and in many cases even this point is lost. The organ is then of an almost uniform opaque yellowish-white colour, and the boundary between the individual lobules may be completely obscured. In very exceptional cases the accumulation of fat is much more abundant in some portions of the liver than in others, so that on section, yellowish points and streaks are seen scattered over its surface. The consistence of the organ is much diminished, it feels doughy, and pits on pressure with the finger, and the knife used to cut it becomes coated with oil. The pressure exercised by the infiltrated fat produces considerable anæmia of the organ, but the interference with the circulation is never sufficient to cause ascites, hæmorrhage, or other evidences of portal congestion.

Fatty infiltration of the liver occurs under two opposite conditions—one in which there is general obesity, and the fat accumulates in the liver in common with other parts; and another, in which there is general emaciation, and the fat is removed from the subcutaneous cellular tissue and from the other situations in which it naturally exists, whilst it accumulates in the hepatic cells. The latter is exceedingly common in chronic pulmonary and cardiac affections, especially in pulmonary phthisis. Possibly in these cases the interference with the respiration, and the consequent incomplete oxidation of the hydrocarbons, is intimately connected with it.

CHAPTER VII.

AMYLOID DEGENERATION.

AMYLOID degeneration, which is one of the most important of the degenerative processes, consists in the infiltration of the tissues with a peculiar homogeneous translucent substance closely resembling albumen, by which their vitality becomes diminished and their functions impaired.

It is often known as the *lardaceous*, or *waxy* change, the organs affected by it having somewhat the appearance of lard or wax. The term "*amyloid*"—which was applied to it by Virchow, from the supposed resemblance of the new material to cellulose or starch—as being that by which it is perhaps most generally known, is here adopted.

This form of degeneration is rarely a primary affection, but usually occurs in the course of some other disease. It appears to be associated with certain cachectic conditions, brought on by many exhausting diseases. It is in those diseases which are attended by profuse and long-continued suppuration, as chronic diseases of bone, empyema, chronic tubercular and other disintegrative diseases of the lungs, chronic pyelitis, and syphilis, that the amyloid change most frequently occurs. In syphilis, it is those cases in which there is caries or prolonged ulceration that it is most commonly met with.

Every organ and tissue may be the seat of the change;

those, however, in which it is especially prone to occur, are the kidneys, the liver, the spleen, the lymphatic glands, and the intestines. It is met with less frequently in the stomach, in the supra-renal capsules, in the pharynx and œsophagus, in the bladder, prostate, and generative organs, in serous membranes, in the membranes of the brain and cord, and in muscle. It is rarely limited to one organ, but several organs are almost invariably simultaneously affected by it.

Respecting the nature of the new material which infiltrates the tissues, the analyses of Kekulé and Schmidt show that it is a nitrogenous substance closely allied to albumen. The conclusions arrived at by these observers are, however, not satisfactory, as they were unable completely to separate the substance from the tissues in which it was deposited. More recently, Kühne has succeeded, by submitting the amyloid organs to a process of artificial digestion, in completely isolating the new material, and the results of his investigations confirm those of Kekulé and Schmidt. The investigations of Dr. Marcet* show that the infiltrated organs are considerably deficient in potash and phosphoric acid, whilst they contain an excess of soda and chlorine. It appears therefore that the amyloid substance is nitrogenous, and that it very closely resembles albumen.

The most characteristic feature of the amyloid substance is the peculiar reaction which it gives with iodine, and with iodine and sulphuric acid. If an aqueous solution of iodine—made with the help of iodide of potassium—be applied to an amyloid organ, the affected portions change to a deep reddish-brown colour : this is not permanent, but gradually passes off, and the part regains its former appearance. If the application of the iodine be followed by the cautious addition of sulphuric acid, a blackish-blue or violet tint is produced. This latter reaction, however, is not easily obtained, considerable nicety being required in the application of the reagents. The following is the method for obtaining it, recommended by Professor Virchow:—A dilute aqueous solution of iodine must be allowed to soak well into the tissue, the excess must be poured off, and a single drop of concentrated sulphuric acid gradually added, when a blue or violet colour will be produced, either at once or after some time. In the hands of English pathologists this latter reaction has certainly met with but little success; and if the colour be obtained, it is by no means satisfactory, and more nearly resembles a black than the blue which has been described. Fortunately, however, the reaction with iodine alone is perfectly characteristic, and the attempt to obtain the blue by the subsequent addition of sulphuric acid, is therefore quite unnecessary. If the change is at all advanced, the reddish-brown colour will be produced by merely pouring the aqueous solution of iodine over the cut surface of the organ; but in slighter degrees of the affection, thin sections must be made with a Valentin's knife, and well washed with water to remove the blood, before the coloration with iodine can be obtained.

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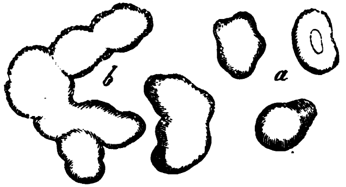
* See "Report of Committee on Lardaceous Disease," Trans. Path. Soc. Lond. 1871.

Upon considering the above reactions, it will be seen that they resemble, in some respects, those exhibited by some well-known organic substances. Cellulose—the substance which forms the external membrane of vegetable cells—yields a blue when treated with iodine and sulphuric acid, and so far resembles the amyloid material; but differs in not being coloured by iodine alone. The same is true of cholesterine; this also gives a reddish-brown with sulphuric acid, but is not altered by iodine. To starch, the resemblance is not so marked as to the two preceding substances: with this, iodine produces a blue colour without the addition of the acid.

The amyloid substance almost invariably makes its appearance first in the small arteries and capillaries, and subsequently extends from them to the surrounding tissues. The cells of the intima and of the muscular coat are the first to become infiltrated, then the remaining structures of the artery. When the vessels have become infiltrated, the amyloid matter extends to the immediately surrounding parts; it invades both the cells and the intercellular substance, and may gradually extend until the whole organ is completely impregnated.

The changes produced in the tissues by this infiltration are very characteristic. The cells as they become filled with the new material gradually increase in size; they lose any irregularities in their contour, and become rounder and more regular in shape; their nuclei disappear, and the whole cell is converted into a structureless homogeneous body, which has a peculiar translucent glistening appearance. (Fig. 14, *a.*) If the cells are in close contact many of them may coalesce, and their distinctive boundaries thus become obliterated. (Fig. 14, *b.*) The intercellular substance in the same way acquires a homogeneous glistening appearance. The walls of the small arteries—in which, as already stated, the change commences—become considerably thickened, and they

FIG. 14.



Liver Cells infiltrated with the Amyloid Substance.
a. Single cells. *b.* Cells which have coalesced. × 300. (Rindfleisch.)

present the same homogeneous translucent characters. The calibre of the vessels is diminished, and the circulation through them is consequently impeded.

Organs in which this change is at all advanced, present features so characteristic that its nature can be readily recognised by the naked eye. They are usually considerably increased in size; their absolute weight is increased, and also their specific gravity; their surface is smooth, and the capsule tense and stretched; their consistence is firm and somewhat elastic. On section they exhibit a peculiar homogeneous, glistening, translucent appearance, somewhat resembling wax or glue. Owing to the diminished calibre of their bloodvessels and to the pressure exercised by the new material, they contain but little blood, and hence are always pale in colour. The change may involve the whole organ, or it may be limited to certain portions. In the spleen, for example, it is frequently limited to the Malpighian corpuscles; and in the liver, to the cells in the immediate vicinity of the hepatic artery.

Although the above characters are often sufficiently marked, they should always be confirmed by the application of iodine to the cut surface of the organ. In slighter degrees of the affection—when the physical characters are but little altered—the application of this reagent becomes necessary in order to discover the presence of the new substance. In these cases, merely pouring the solution over the organ will often fail to produce the characteristic staining; and it will be necessary to make thin sections with a Valentin's knife, and wash them thoroughly with water to remove the blood, before the reaction can be obtained.

In the earliest stages of the change the use of the microscope may be necessary for its recognition, and by this means the slightest degrees of it can be readily discovered. If thin sections of the tissue are examined, those parts which are infiltrated will present the peculiar homogeneous translucent appearance already described, the cells having lost their distinctive characters, and being united with the intercellular substance into a more or less uniform mass. The addition of iodine wlll render, by the staining, any change at once apparent.

The effect of amyloid degeneration is to impair or even to completely destroy the nutrition and function of those organs which are affected by it. This is owing to two causes—the obstruction offered to the circulation, and the direct influence of the new material upon the parenchyma of the organ. The obstruction to the circulation, which results partly from the diminution in the calibre of the small arteries, and partly from the general pressure exercised by the infiltrated substance, causes an insufficiency in the supply of arterial blood. As a consequence of this, secondary atrophic changes are induced in various parts; the cells atrophy and often undergo fatty metamorphosis, which indeed is frequently associated with the amyloid change. The infiltration of the parenchyma of the organ impairs the vitality of the cellular elements, and may ultimately completely arrest any manifestation of their functions.

As this form of degeneration is almost invariably secondary to some grave constitutional state, it can rarely be looked upon as in itself a cause of death, although it may materially hasten, and even determine the fatal termination.

Having thus described the nature of the amyloid substance, and the way in which it makes its appearance in the several tissues of an organ, it remains to consider the source from which it is derived. The disease, as already stated, appears to be an infiltration, and to consist in the deposition of a new material from the blood in the various tissues and organs. The existence, however, of any albuminoid substance in the blood which resembles amyloid in its reaction with iodine, has never been made out, even in the most marked cases of the disease. This fact must therefore negative the supposition that it is a simple infiltration. If the new material be derived from the blood at all, it must undergo some chemical change subsequently to its deposition in the tissues. Dr. Dickinson considers that it is dealkalized fibrin, which is deposited in consequence of the loss of the alkali with which it is normally combined; this loss resulting from the profuse suppuration to which the disease is usually secondary:—hence he terms it "*depurative infiltration.*"* Whether this be so or no, it is probable that some abnormal condition of the blood is the cause of the disease, and that the change itself consists in the retention and coagulation in the tissues of some albuminoid substance which is derived from the nutritive fluids. Whether this is albumen or the fibrinogenous substance is unknown. The way in which the several tissues of an organ are affected, the change almost invariably commencing in the small nutrient blood-vessels, and extending from them to the surrounding parts; the general character of the affection, several organs being simultaneously involved; together with the fact that it is almost invariably secondary to chronic suppurative diseases—point to some alteration in the composition of the blood as the cause of the degeneration.

AMYLOID DEGENERATION OF THE LIVER.

The liver is one of the most frequent seats of the amyloid change, and here, as in other parts, it commences in the small nutrient blood-vessels. The minute branches of the hepatic artery are first affected, and from these the infiltration gradually extends to the hepatic cells immediately adjacent, until ultimately the whole organ may become involved.

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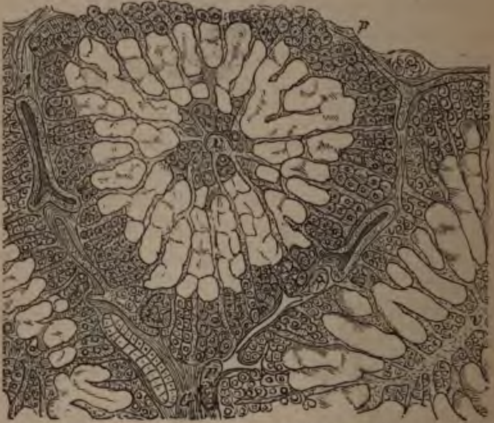
* "Medico-Chirurgical Transactions," vol. 1.

If a liver be examined in the early stage of the affection, and the iodine solution applied to thin washed sections of the organ, it will be found that the characteristic staining is limited to certain portions of the lobules—viz., to those which are situated between their external and central parts. This intermediate portion corresponds with the distribution of the hepatic artery, and the hepatic cells situated between its ramifications being infiltrated with the new material before those in the external and central portions of the lobule, the brown staining is first apparent in this situation. (Fig. 15.)

FIG. 15.



Amyloid Liver. Showing the infiltration of the cells in the intermediate zone of the lobule. *A.* Interlobular artery. *V.* Hepatic vein. *pp.* Portal vessels. × 300. (Rindfleisch.)

The earliest seat of the amyloid change thus differs from that of the fatty. In fatty infiltration it is the most external portion of the lobule in which the fat accumulates—that which corresponds with the distribution of the portal vein (see Fig. 13). It differs also from the infiltration with pigment, which takes place in the most central portion, around the hepatic vein. Thus in each hepatic lobule three zones may be distinguished:—an external one, which is the chief seat of the fatty change; a central one, which is the chief seat of the pigmentary change; and an intermediate one, which is the chief seat of the amyloid change. These three zones, indeed, may frequently be recognised by the naked eye, the pale opaque external one contrasting strongly with the intermediate one which is translucent, and with the darker central one. In the most advanced stages of the disease, however, both the external and central portions of the lobule may become involved, and the cut surface present an almost uniformly homogeneous appearance.

The amyloid liver is increased in size, often very considerably so; it may be so large as almost completely to fill the abdominal cavity. The enlargement is uniform, and hence the natural configuration of the organ is but little altered. Its weight is increased, and also its specific gravity. Its edge is rounded, the surface is smooth, and the capsule appears tense and stretched. The consistence is firm and elastic. The cut-surface is dry, bloodless, smooth, translucent, and waxy-looking, and of a pale reddish-grey or dirty yellow colour. If the change is very far advanced, the tissue may be perfectly homogeneous, all distinction between the individual lobules being lost. In other cases the lobules are distinctly mapped out; they are enlarged, and the external zone may be of an opaque yellowish-white colour owing to the presence of fat. This association of the fatty and amyloid changes is exceedingly common. Amyloid infiltration does not obstruct the portal circulation, and hence does not cause ascites. It impairs the vitality of the hepatic cells, and thus interferes with the functions of the organ.

AMYLOID DEGENERATION OF THE KIDNEYS.

The kidneys are especially liable to be involved in the amyloid change, and are frequently the earliest seats of the morbid deposition. It may constitute in them the primary lesion, or it may occur subsequently to inflammatory conditions of the secreting and interstitial structures. As a primary change it is one of the most important varieties of Bright's disease.

The process commences in the tufts of vessels which form the Malpighian bodies, the walls of which become thickened by the infiltration of the new material, so that the tufts are increased in size. It then proceeds to the small afferent arteries, and ultimately to the vasa efferentia, and to the arteriolæ rectæ which run through the medullary portion of the organ. After these vessels have thus become infiltrated, and before those in the pyramids are affected, the deposition extends to the intertubular tissues of the cortex, into which the amyloid substance is poured, imbedding the tubuli uriniferi in its course. In some parts it appears that the exudation takes place into the tubes themselves, as the casts which they contain are occasionally deeply stained by the iodine solution: this, however, is far from being frequently the case. In the earlier stages of the process,—if the organ is not the seat of any other morbid change—the tubes and their lining epithelium present a perfectly natural appearance. Many of them contain pale hyaline casts, which also appear in the urine. These, however, are probably simply albumen and fibrin which have transuded from the vessels; although from the reaction they occasionally exhibit, it appears that they sometimes consist of the same material as that which permeates the vessels and intertubular structures. As the change proceeds, and the new material increases in amount, the tubes become compressed, and in many places completely obstructed. If the compression is not uniform, they may dilate and form small cysts. The epithelium, which was at first normal, ultimately atrophies and undergoes fatty changes, owing to the interference with its nutrition. In some cases it appears to be the seat of a catarrhal condition, and the tubes are found blocked with epithelial products.

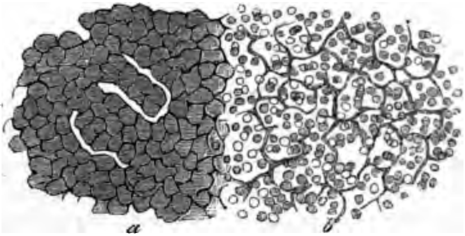
The first effect of this change is to obstruct the circulation in the cortex. The blood-vessels, diminished in calibre, allow little but the liquor sanguinis to pass through them, the passage of the blood-corpuscles being to a great extent prevented: hence the pallor of this portion of the organ. The arterial walls are so altered that fluids and albumen readily permeate them; and thus is produced the large quantity of urine, loaded with albumen, which characterizes the earlier stages of this affection. As the infiltration increases, and the tubes become obstructed, the urine diminishes in quantity. The excretion of urea is less interfered with than in other forms of Bright's disease, and hence symptoms due to its retention seldom occur. Tube casts are rarely numerous; they are for the most part hyaline and finely granular, though sometimes they contain fatty epithelium.

In the earlier stages of the affection, the cortex of the kidney is merely rather paler than natural, and perhaps somewhat firmer in consistence; but otherwise it presents no abnormal appearance. It is only upon the application of iodine to the cut surface, or to thin washed sections of the organ, that its diseased condition becomes evident. When this test is employed, the Malpighian bodies at once become apparent as minute red points scattered through the cortex. As the disease advances, the size of the organ increases; the enlargement, however, is principally confined to the cortex. The surface is smooth, and *the capsule* separates readily. The enlarged *cortex is remarkably* pale and anæmic, and has a peculiar translucent, homogeneous, wax-like appearance. Its consistence is hard and firm. A few scattered vessels may be seen on the surface, and the bases of the pyramids sometimes exhibit an increased amount of vascularity. If iodine be poured over the cut surface, the Malpighian bodies and the arteries of the cortex become mapped out almost as clearly as in an artificial injection. The enlarged Malpighian bodies may indeed often be seen as glistening points before the iodine is applied. Frequently, the homogeneous appearance of the cortex is interrupted by minute, opaque, yellowish-white lines and markings; these are produced by the fatty changes in the epithelium of the tubes, which so commonly occur in the later stages of the affection. Ultimately, the capsule may become more or less adherent, and slight irregular depressions may make their appearance on the surface of the organ: the latter are due to atrophic changes in some of the tubes. If, as is not unfrequently the case, the infiltration is associated with an increase in the intertubular connective tissue, the atrophy of the organ will be more marked. (See " Interstitial Nephritis.")

AMYLOID DEGENERATION OF THE SPLEEN.

Amyloid degeneration of the spleen is met with in two forms—one in which the disease is limited to the Malpighian corpuscles (" Sago Spleen"), and the other in which the pulp appears to be chiefly implicated. The former is much the more common condition. In it the Malpighian corpuscles become infiltrated with the amyloid substance and converted into translucent wax-like bodies, much like boiled sago:—hence its name. The process commences in the small arteries of the corpuscle, and it is only after these have become infiltrated that it extends to the corpuscles themselves. The small lymphatic cells of which the corpuscle is made up are then involved in the process, they increase in size, become more irregular in outline, many of them coalesce, and ultimately the whole is converted into a pale, firm, translucent, glistening mass. (Fig. 16.)

FIG. 16.



Amyloid Degeneration of the Spleen—"Sago Spleen." A portion of one of the infiltrated Malpighian corpuscles *a*, with the adjacent normal splenic tissue *b*. Showing the increase in size, and in many parts, the coalescence of the cells, of which the corpuscle is composed. × 200.

The sago spleen is more or less enlarged; its weight and density are also increased. The cut surface is smooth, dry, and studded all over with small glistening sago-like bodies, varying in size from a millet to a hemp-seed, which are stained a reddish-brown colour by the iodine solution. These may become so large as to occupy a large portion of the organ, although in earlier stages of the affection they are so minute that they can only be seen in thin sections of the tissue.

In the other variety of amyloid spleen, the pulpy parenchyma between the corpuscles is infiltrated with the new material. This is probably merely an advanced stage of the former condition, in which the disease extends from the corpuscles to the surrounding pulp; the whole organ being ultimately involved. Under these circumstances the organ often attains a considerable size, much larger than is met with in the sago spleen. It is remarkably hard and firm, and the capsule is tense and transparent. On section it presents a dry, homogeneous, translucent, bloodless surface, of a uniform dark reddish-brown colour. Thin sections can be readily made with a knife, the organ cutting like soft wax. The corpuscles are not visible as in the former variety, being probably obscured by the surrounding pulp, which has become so densely infiltrated with the amyloid substance.

AMYLOID DEGENERATION OF LYMPHATIC GLANDS.

In the lymphatic glands the process much resembles that in the spleen. The small arteries in connexion with the follicles of the gland are the earliest seats of the change; and from these it extends to the minute cells with which the follicle is filled. The follicle thus becomes ultimately converted into a small homogeneous mass.

The glands are enlarged, and on section the minute wax-like bodies can often be seen scattered through the cortex. The cut surface is smooth, pale, and translucent.

As these glands are largely concerned in the formation of the blood-corpuscles, their implication in the amyloid change must to a large extent aid in producing the emaciation and anæmia which characterize this affection. The same is true of the spleen, which is usually simultaneously involved.

AMYLOID DEGENERATION OF THE ALIMENTARY CANAL.

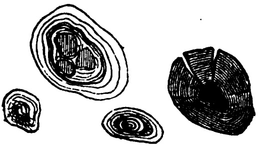
The whole of the alimentary tract may be the seat of the amyloid change, and here it assumes an important aspect from the deleterious influence which it exercises upon the absorbent and secreting processes, and from the consequent impairment of the general nutrition which results. The disease, however, in this situation is very apt to escape observation, as it produces but little alteration in the appearance of the parts. The mucous membrane may look somewhat pale, translucent, and œdematous, but otherwise to the naked eye nothing is discoverable. It is only upon the application of iodine to the washed mucous surfaces that the nature of the change becomes apparent. In the small intestine—which is perhaps the part most commonly affected—the effect of the application of iodine is very characteristic. A number of small reddish-brown points appear over the whole surface of the membrane; these correspond to the intestinal villi, the arteries and capillaries of which are infiltrated with the amyloid substance. In the stomach and œsophagus the vessels are mapped out in a similar manner by the iodine solution. The change in the intestine gives rise to serous diarrhœa, this being probably due to an increased permeability of the infiltrated walls of the vessels.

THE CORPORA AMYLACEA.

The corpora amylacea or "amyloid bodies," so frequently met with in the nervous system, in the prostate, and in other parts, have usually been looked upon as more or less allied to the amyloid substance; there appears, however, with the exception of a certain similarity in their behaviour with iodine and sulphuric acid, to be no connexion between them.

They are round or oval bodies, formed of a succession of concentric layers, and are often changed to a deep blue colour by iodine, thus bearing both in their structure and chemical properties the strongest resemblance to granules of vegetable starch. (Fig. 17.) Sometimes, however, the blue is only exhibited after the subsequent addition of sulphuric acid, and thus a resemblance is shown to the amyloid substance.

FIG. 17.



Amyloid Bodies from the Prostate.

They vary in size from microscopic granules, to bodies which are distinctly visible to the naked eye; sometimes being as much as one or two lines in diameter. The larger ones are usually formed by the conglomeration of the smaller granules, which are often enclosed by a common envelope.

They occur especially in the nervous system of those in advanced life; the ependyma of the ventricles, the white substance of the brain, the choroid plexus, the optic nerve and retina, and the spinal cord, being their favourite seats. The larger forms are met with most frequently in the prostate. The prostate of nearly every adult contains some of these bodies; and they may accumulate here to such an extent as to form large concretions. They are also occasionally met with in the lungs, and in mucous and serous membranes.

As has been said, they usually exhibit a bright blue colour upon the application of iodine alone, although in some cases not until the subsequent addition of sulphuric acid. Many of them, however, are coloured green, or even brown by these reagents. The green is due to their admixture with nitrogenous matters, which give a yellow colour with iodine, and hence the combination yields a green. The greater the amount of nitrogenous matter the more brown does the colour become.

From the laminated structure of these bodies they would appear to be formed by the gradual precipitation of some material, layer by layer, upon the surface of pre-existing particles. The nature of the material, however, does not appear to resemble that of the substance which infiltrates the organs in amyloid degeneration. The two processes are so essentially different, both in the circumstances under which they occur and in the characters and seat of the morbid products, that they cannot be looked upon as in any way analogous. Amyloid degeneration is a general change, in which numerous organs become infiltrated with an albuminoid substance, whereas the formation of the corpora amylacea is evidently of a local nature. The latter is often preceded by those local atrophic changes associated with advanced life, and consists in the deposition of some starch-like material, probably liberated in the tissues themselves, upon any free body which may exist in its vicinity.

The corpora amylacea, especially those occurring in the choroid plexus and in the lateral ventricles, are very liable to become calcified, and they then constitute one form of "brain sand" which is so often met with in these situations.

CHAPTER VIII.

CALCAREOUS DEGENERATION.

CALCAREOUS Degeneration—or, as it is more commonly called, *Calcification*—consists in the infiltration of the tissues with calcareous particles. Physiologically, an infiltration of calcareous particles takes place in the formation of bone, in which lime and magnesian salts are deposited in the fibrous or cartilaginous matrix. This physiological is precisely similar to the pathological process. It is important, however, to distinguish simple calcification from ossification. In the latter there is not only a deposition of lime salts, but an *active* change in the tissue itself—a proliferation of the cellular elements, an intimate union of the calcareous matters with the tissue, and the formation of a true osseous structure in which the calcareous particles are not visible. Calcification, on the other hand, is a purely *passive* process, there is no increased nutritive activity of the part, no multiplication of elements, no alteration of the structure, but merely an infiltration with calcareous particles.

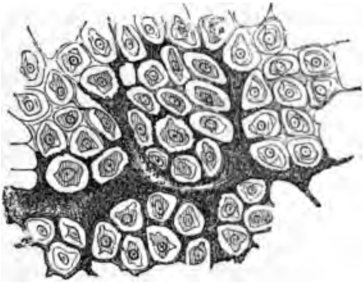
An infiltration and deposition of calcareous substances occurs under two opposite conditions; one—in which there is an absolute increase in the amount of these constituents in the blood, and the excess becomes deposited in the tissues; the other—in which there is no such increase, but the deposition takes place owing to some alteration in the tissue itself.

An absolute increase of the saline constituents in the blood, and the deposition of the excess in the tissues, is much the less frequent form of calcification. It occurs in some forms of softening of bone, especially in extensive caries and osteomalacia. In these diseases the lime salts are removed from the bone, returned into the blood, and deposited in other tissues. In such cases the calcification is usually more or less general—many organs being simultaneously involved. In osteomalacia, it is not uncommon to find the kidneys, the lungs, the stomach, the intestines, and even the dura mater and liver, infiltrated to a greater or less extent with lime salts. The excess of saline matters in the blood may also be due to interference with their excretion by the kidneys. In chronic structural disease of these organs, calcification may sometimes result from the consequent impairment of their excreting functions. To whichever of these causes the excess is due, the deposition will commence in the tissue immediately surrounding the blood-vessels from which the calcareous matters are derived:—thus, in the lungs, the seat of the change is the interlobular tissuc; in the stomach, the stroma between the glands; and in the kidney, the tubuli uriniferi and the intertubular tissue. If the process is the result of impaired excreting function of the kidneys, it may be limited to them; the pelves, and the tubes of the papillæ and pyramids, being the earliest seats of the deposition. Precisely analogous to this form of calcification is the deposition of the excess of urate of soda which takes place in gout.

In the great majority of cases, however, calcification is a *local* change, depending not upon any alteration in the composition of the blood, but upon changes in the tissues themselves, owing to which some of the saline matters which are normally held in solution in the blood are deposited in them. The alteration in the tissues consists in some impairment of their nutrition, associated with a diminution in the amount of blood, and a retardation of its circulation. All those conditions which tend to produce atrophic and retrogressive changes in a part, and at the same time to interfere with the circulation in it, are liable to be followed by its calcification. Inflammation, rapidity of growth, diminished nutritive supply, and general impairment of vitality, may all of them give rise to this process. This is seen in the calcification of the vegetations in endocarditis, of the caseous masses in the lungs and lymphatic glands, of many new formations, and of the blood-vessels and cartilages in old people. In its morbid antecedents calcification thus somewhat resembles fatty degeneration, and its pathological signification is in many cases equally difficult to determine. Fatty degeneration indeed very frequently precedes the calcification, which is merely a later stage of the retrograde process.

Respecting the cause of the deposition of the calcareous substances in the atrophied structures—it is probably partly owing, as stated by Rindfleisch, to the stagnation of the nutritive fluids in the part, owing to which the free carbonic acid which appears to hold the salts in solution, escapes, and they are consequently precipitated; and partly to the non-assimilation of these fluids by the degenerated elements of the tissue. The calcareous particles make their appearance both within the cells and in the intercellular substance; they are much more frequent, however, in the latter situation. They are seen at first as fine molecules scattered irregularly through the intercellular substance. (Fig. 18.) They are characterized, when viewed by transmitted light, by their opacity, dark black colour, and irregular outline, and also by their solubility in dilute mineral acids. They gradually increase in number until ultimately large tracts of tissue may be converted into an opaque calcareous mass, in which the cells are enclosed and can no longer be recognised. These larger masses have a sharp black irregular outline, and when the calcification is complete, acquire a homogeneous, glistening, semi-transparent appearance. The cells themselves are much less frequently infiltrated, being usually merely enclosed and obscured by the calcified intercellular substance. Calcareous particles may, however, make their appearance in the cell-contents, and gradually increasing, convert the cell into a homogeneous calcareous body.

FIG. 18.



Calcified Cartilage. Calcification of the intercellular substance. + 300. (Rindfleisch.)

The calcareous matters consist for the most part of lime and magnesian salts, especially the phosphates and carbonates. If the latter are present, the addition of a little dilute hydrochloric acid is followed by the appearance of numerous minute air bubbles in the tissue, owing to the liberation of carbonic acid. In those cases in which calcification is associated with retained gland-secretions, the calcareous matters will consist of the specific gland salts.

A part which has become calcified undergoes no further change, its vitality is completely destroyed, and it remains as an inert mass. In this respect calcareous differs from fatty degeneration. In the latter, subsequent changes invariably take place; the part either softening, caseating, or becoming the seat of calcification itself. It differs also in its effect upon the tissue. The structure of the affected part is not destroyed, and there is no annihilation of histological elements, such as occurs in fatty degeneration. The tissue is simply impregnated with calcareous matters, which have no other effect upon it than to render it inert; its vitality is destroyed, but its structure—in so far as the calcification is concerned—remains unaltered. If the saline matters are dissolved out with a little dilute mineral acid, the structure of the part may be again recognised, unless, indeed—as is often the case—it has been destroyed by any antecedent change.

Calcification must thus be looked upon in many cases as a salutary lesion, the impregnation with calcareous matters preventing subsequent changes in the part. This is especially the case when it is secondary to other forms of degeneration. It is the most favourable termination of the large class of fatty changes, as is exemplified by the calcification of many inflammatory products, of tubercle, and of many other new formations. It may, on the other hand, under certain circumstances, be attended with most deleterious consequences, as is the case when it affects the arterial system.

CALCIFICATION OF ARTERIES.

Calcification of arteries, like fatty degeneration, may be a *primary* or *secondary* affection. As a secondary change it constitutes one of the terminations of the atheromatous process, and as such is constantly met with in the aorta and its branches, and in many other situations. (See "Atheroma.")

Primary calcification is less frequent than that which occurs in atheromatous vessels. It is essentially a senile change, and is the result of that general impairment of vitality which exists in advanced life. It is associated with atrophy of the arterial tissues, and in some cases with fatty degeneration. As it is not dependent upon a local cause, but upon general malnutrition, the change is a more or less general one, and when occurring in one part is met with in others. It is, however, especially frequent in the superficial arteries, in the arteries of the upper and lower extremities, and in those of the brain. Its most common seat is the middle coat, where it commences in the muscular-fibre cells. The calcareous particles make their appearance at first around and within the nucleus, and gradually increase until they fill the cell, which becomes converted into a small calcareous flake. The process may go on until the muscular coat is completely calcified, or it may be limited to isolated portions of the coat, giving rise to numerous calcareous rings and plates which are irregularly distributed throughout it. From the muscular, it may extend to the external and internal coats, until ultimately the vessel becomes calcified throughout. In the majority of cases, however, the middle coat only is involved.

The vessel thus calcified, loses its elasticity and contractility; its lumen is diminished, and it is transformed into a hard, rigid, brittle tube. This condition is exceedingly common in the external iliac and in the vessels of the lower extremity, where it is a frequent cause of senile gangrene. (See "Senile Gangrene.")

CHAPTER IX.

PIGMENTARY DEGENERATION.

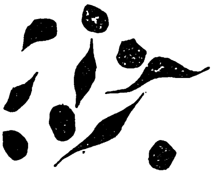
PIGMENTARY Degeneration, or Pigmentation, consists in an abnormal formation of pigment in the tissues. All true pigments are derived from the colouring matter of the blood. Physiologically, many of them are eliminated by the kidneys and liver; others are deposited in the tissues, and there remain permanent. The choroid coat of the eye and the skin of the negro, are well-known examples of tissues in which there is this permanent accumulation of pigment. The cells in these situations appear to be endued with a special power to abstract the colouring matters from the blood, and to store them up in their interior, where they undergo certain chemical changes and become converted into pigment.

In the pathological process also, the pigment is derived from the same source, although its presence in the tissues is rarely dependent upon any abnormal secreting powers in their cellular elements, but is usually the result of certain changes in the circulation or in the blood-vessels, owing to which the colouring matter of the blood escapes and infiltrates the surrounding parts. This escape of hæmoglobin may be owing to rupture of the vessels themselves, or to conditions of congestion or stasis, in which the blood-corpuscles and liquor sanguinis pass through their walls. In either case the hæmoglobin will permeate the tissues and ultimately be converted into pigment. Rupture of the vessels and the direct extravasation of blood, is, however, the most common antecedent of the pigmentary change. Soon after the extravasation has taken place, the hæmoglobin escapes from the red blood-corpuscles, either by exudation or by destruction of the corpuscle, and mixed with the liquor sanguinis, infiltrates the surrounding tissues. In other cases it escapes without any solution of continuity in the walls of the vessel. This frequently occurs in conditions of inflammatory stasis and mechanical congestion, in which serous exudation takes place into the tissues, and the hæmoglobin is liberated from the blood-corpuscles within the vessels, from which it transudes, dissolved in the liquor sanguinis. Lastly, the red corpuscles themselves may pass through the walls of the capillaries without rupture having taken place. In whichever of these ways the solution of hæmoglobin is derived, it infiltrates the tissues, staining both the cells and the intercellular substance a yellowish or brownish-red colour. It is taken up, however, more readily by the cells than by the intercellular substance, or by membranous or fibrous structures; and it stains only the cell-contents, the nucleus and cell-wall remaining unaltered.

After the colouring matter has remained for some length of time in this diffuse form, it undergoes certain changes:—it becomes darker and more or less granular, minute reddish-brown or black granules and crystals make their appearance both in the cells and in the intercellular substance, and these may gradually increase and form larger masses. This change in the extravasated hæmoglobin is a chemical one, and the substance into which it is converted is *hæmatoidin.* Hæmatoidin appears to be closely allied to the colouring matter of the bile, *cholepyrrhin,* which is also a derivative of hæmoglobin. It exhibits similar reactions when treated with concentrated mineral acids, displaying the same variations of green, blue, rose, and yellow colours. It is insoluble in water, alcohol, ether, and in dilute mineral acids and alkalies; it is soluble in the caustic alkalies giving a red colour. It contains more carbon than hæmoglobin; and it also contains iron.

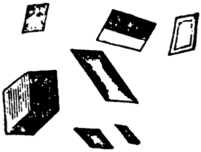
The granules of hæmatoidin vary in size from the smallest particles to masses as large as a red blood-corpuscle. The larger ones are round, or more commonly irregular in shape, and have a sharp defined border. Their colour varies from yellow, red, and brown, to black. These variations appear to depend upon the age of the granules and the tissue in which they are formed; the older they are the blacker they become. The smaller granules are usually dull and opaque, the larger ones, however, often present a more or less glistening appearance. (Fig. 19.) The crystals of hæmatoidin are oblique rhombic prisms, usually of a beautiful yellowish-red or ruby-red colour, sometimes approaching to brown or black. They may also occur as little plates and fine needles, but these are less common forms. (Fig. 20.) They are in most cases so small that considerable care is required to recognise their crystalline nature under the microscope, and they may easily be overlooked as merely irregular granular masses: in some cases, however, they

FIG. 19.



Cells containing pigment. From a melanotic sarcoma of the liver. × 350.

FIG. 20.



Hæmatoidin crystals. (Virchow.)

attain a larger size. They are more or less transparent, and present a shining strongly refracting surface.

Whether the hæmoglobin is converted into granular or crystalline hæmatoidin appears partly to depend upon the tissue in which it is situated, the crystals being exceedingly common in some situations, as in the brain and ovaries, whereas in others, as the lungs, only the granules are met with. Both the granules and crystals are characterized by their durability and by their great powers of resistance; when once formed they undergo no further change.

Those forms of pigment—both granular and crystalline—which are of an intensely black colour, have been supposed to consist of a substance which differs in chemical composition from hæmatoidin, and which has been called *melanin*. There appears, however, to be no foundation for such a distinction. Melanin is probably merely hæmatoidin, which has become more or less altered by age. It is endued with greater powers of resistance, being less readily soluble in reagents than the more recently formed hæmatoidin.

Pigmentation, although one of the most common and universal forms of degeneration, is of comparatively little importance as a morbid process. The mere existence of pigment within and between the histological elements of the tissues, has in itself but little influence upon their vitality and functions. The atrophy and impairment of function which so frequently accompany it, must rather be looked upon as the result of those conditions upon which the formation of the pigment depends, than as in any way owing to the presence of the pigment itself.

As evidence of other antecedent conditions, pigmentation assumes a more important aspect. The pigment being derived from extravasated hæmoglobin, in whatever situations it *occurs, it* must be looked upon as the result of *some alteration* in the circulation or in the blood-vessels, owing to which the escape of the colouring matter is permitted. Exceptions to this exist, however, in the case of certain pigmented new formations, in which the presence of the pigment appears to be mainly owing to the selective power of the cells; these, like those of the choroid, separating the colouring matter from the blood. It is those growths which originate in tissues normally containing pigment, as the choroid and rete mucosum, which are most frequently melanotic. (See "Melanotic Sarcoma.") In Melanæmia, again, the large quantities of pigment which exist in the blood, are the result of a local formation —for the most part by the spleen. Lastly, in Addison's disease, the pathology of the pigmentation of the skin is at present involved in obscurity.

Pigment is often the only evidence of a former extravasation. This is frequently the case in cerebral hæmorrhage, where the crystals of hæmatoidin may be all that remains to indicate that rupture of the capillaries has taken place. In the ovaries, also, the slight hæmorrhage which follows the escape of the ovum at each menstrual period, is marked by the formation of pigment which constitutes the "corpus luteum." In mechanical congestion and inflammation, again, the consequent pigmentation may be the principal evidence of the former existence of these conditions: this is especially seen in pigmentation of the mucous membrane of the stomach and intestines. The formation of pigment is thus, with the few exceptions above named, the result of some antecedent change in the blood-vessels or circulation; and its presence in the tissues appears to be little more than a testimony to the existence of those processes upon which its formation depends.

False Pigmentation.—There are certain forms of discoloration of the tissues which are not due to the presence of hæmatoidin: these must be distinguished from true pigmentation. The most important of them, and that which is most closely allied to the process already described, is the staining of the tissues with the colouring matter of the bile, which is itself a derivative of hæmoglobin, and is, as before stated, very analogous to hæmatoidin. This yellow staining may affect nearly all the tissues, constituting "jaundice;" or it may occur in the liver alone, from local obstructions to the small bile-ducts, as is often seen in cirrhosis of that organ. In these cases, however, there is merely the staining of the tissues with the colouring matter of the bile, and no subsequent conversion of this into pigment.

The discoloration caused by the long-continued use of the salts of silver must also be distinguished from true pigmentation: the colour here is due to the deposition of the silver in the tissues. The black colour of gangrenous parts, and that sometimes produced by the effusion of large quantities of blood into the tissues, must again not be confounded with pigmentation; the discoloration in these cases is the result of the action of the sulphuretted hydrogen upon the colouring matter of the blood. The greenish-black discoloration so often seen on the surface of the liver, kidneys, and other abdominal organs after death, is in the same manner due to the intestinal gases. Lastly, the minute particles of inhaled carbon which are always met with in the lungs, must be distinguished from true pigment.

PIGMENTATION OF THE LUNGS.

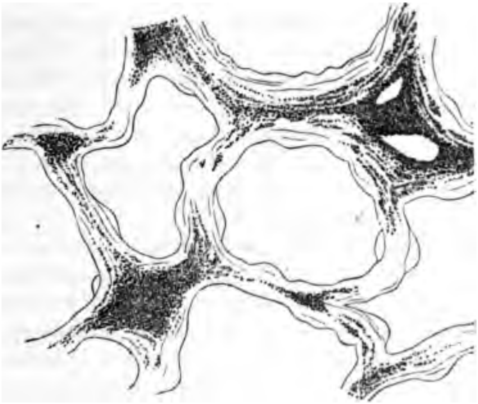
In no organs is pigment met with so frequently and in such large quantities as in the lungs, and here much discussion has arisen as to its nature and origin. The lungs normally contain more or less black pigment, the amount of which gradually increases with advancing age—the lungs of infants and young children being almost free from it, whereas those of adults invariably contain it in *considerable quantities.*

This normal pigmentation of the lungs is principally due to the presence of carbon, and not to that of true hæmatoidin-pigment. The carbon—which is derived from the incomplete combustion of wood, coal, and other substances, and is always present in varying quantities in the atmosphere—is inhaled, and the minute particles pass into the finest bronchial tubes. Having entered the bronchi, many of them are taken up by the mucus-corpuscles, where they may be seen as small black granules within the cells. These may readily be observed in the cells of the greyish-black sputum which is so frequently expectorated in the early morning. Much of the carbon thus inhaled is eliminated by expectoration; many of the particles, however, pass into the air-vesicles, and here their removal by this means being less readily effected, they gradually penetrate the pulmonary substance, and make their way into the alveolar walls and inter-lobular tissue. It is in these situations that most of the pulmonary pigment is found, and there it may be seen either within the connective tissue-cells, or lying free amongst the fibres.

As to the means by which the particles of carbon penetrate the walls of the air-vesicles and minute bronchi, nothing is certainly known. They are probably conveyed by amœboid cells, and by the extra-vascular nutrient fluids. Be this as it may, there can be no doubt that the penetration takes place, this having been conclusively demonstrated by physiological experiment. When once the carbon has made its way into the inter-lobular tissue, some of it is taken up by the fixed cells in this situation, whilst that which is not thus detained, passes on to the lymphatics, and is deposited in the bronchial lymphatic glands, where the black particles are also visible.

Closely allied to this physiological pigmentation of the lung from the inhalation of carbon, are those morbid conditions which result from the inhalation of particles of coal, stone, iron, and other substances,—of which the lungs of miners, stone-masons, and grinders afford frequent examples. Here also minute particles enter the bronchi, penetrate the pulmonary substance, and are deposited principally in the inter-lobular tissue. In the case of miners—in which this is most common—the particles of coal enter the lungs in such large quantities as to give to them a uniform dark black colour, and like the carbon normally inhaled they are most abundant in the interstitial tissue. (Fig. 21.) In stone-masons, grinders, &c., the lungs also become deeply pigmented, although to a less extent than those of miners.

FIG. 21.

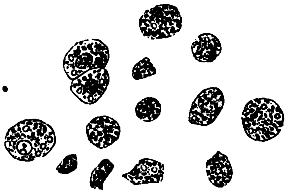


Colliers' lung, showing particles of carbon in the alveolar walls and inter-lobular tissue. × 300. (Rindfleisch.)

The black colour of the lungs in these cases, however, is not entirely due to the presence of the inhaled substances, but partly to that of true hæmatoidin-pigment. The inhalation of the *irritating* particles sets up inflammatory *changes in the bronchi* and pulmonary tissue, causing chronic bronchitis, chronic lobular pneumonia, and a large increase in the fibrous tissue of the lungs, which thus ultimately become consolidated, excavated, tough, and fibrous ("Colliers" and "Knife-grinders' Phthisis," &c.) Owing to these structural changes there is a considerable escape of colouring matter, either from rupture of the capillaries or transudation of serum, and hence a large formation of true pigment; and to this true pigment much of the dark colour of these lungs must undoubtedly be ascribed. The lungs of stone-masons and grinders are, like those of miners, deeply pigmented, although to a less degree, but the black colour in the former cases cannot be entirely accounted for on the supposition that it is due to the presence of inhaled particles.

Pigmentation of the lungs from the presence of hæmatoidin occurs as the result of many other morbid conditions, many diseases of these organs being attended by the formation of pigment. In chronic phthisis, pigmentation occurs, partly as the result of the inflammatory process, and partly from the obstruction of the vessels caused by the new growth:—lines of pigment are constantly seen surrounding the nodules of consolidation. In acute croupous pneumonia, the blood which is extra-

Fig. 22.



Cells from the sputum of acute Bronchitis. Showing the minute granules of pigment within the cells. Some of the cells also contain a few fatty molecules. × 400.

vasated into the air-vesicles, and which in the early stages gives to the expectoration a rusty or prune-juice colour, subsequently becomes converted into pigment, and the sputum becomes of a greyish-black; the pigment granules being visible in the newly-formed cells. The cells met with in the sputum of bronchitis also contain granules of pigment (Fig. 22); and pigmentation plays an important part in the condition of the lungs known as brown induration. (See "Brown Induration of the Lungs.")

Pigment in the lung usually occurs as black irregular granules; it is rarely met with in a crystalline form. In all cases in which it is found in any quantity in the lung, it is also found in the bronchial glands. It is taken up by the lymphatics and, like the inhaled carbon, it becomes arrested in its passage through these glands, where it remains permanently.

CHAPTER X.

NUTRITION INCREASED.

THE morbid changes thus far described, have been attended either by *arrest* or by *impairment* of nutrition;—those remain to be considered in which the nutritive activity is *increased.* They include Hypertrophy and the New Formations.

HYPERTROPHY.

Hypertrophy is an increase in the amount of a tissue, resulting from an increase in its functional activity. The increased functional activity, and the consequent hypertrophy, are in most cases *conservative* in their nature, being induced by some necessity for an increased manifestation of the functions of the tissue; in muscle, for example, in order to overcome some obstruction; in a secreting organ, to secrete more fluid.

It is in muscular tissue that hypertrophy is most frequently met with. Examples of it are furnished by the hypertrophy of the muscles of the calf in ballet dancers; also by the hypertrophy of a hollow viscus from obstruction to the exit of its contents—as of the heart from obstruction at the valvular orifices, or in the course of the circulation, of the muscular coat of the stomach in stricture of the pylorus, of the intestine above a permanent stricture, and of the bladder in stricture of the urethra. The kidney also may become hypertrophied, owing to the loss or incapacity of its fellow. In bone, hypertrophy of the fibula has been observed in cases of disease, or of ununited fracture of the tibia. In all these cases the necessity for increased activity leads to increased development.

The term "hypertrophy" is frequently applied to those enlargements of organs which result from long-continued irritation, or from other unknown causes; as to enlargements of the lymphatic glands, of the tonsils, the thymus, and of the prostate gland. Such growths, however, are some of them inflammatory in their nature, others come more properly within the category of "tumours." It is better, in order to avoid confusion, to limit the use of the term "hypertrophy" to those conservative growths which result from increased functional activity of the tissue.

The increase in the amount of the tissue may be owing simply to an increase in the *size* of the elements of which it is composed: it is then termed *simple* hypertrophy. The process, however, is usually more complex, the increased nutritive activity of the elements which leads to an increase in their *size*, leads also to an increase in their *number*, and to the formation of a new tissue, which is similar to that from which it originated:—this is termed *numerical* hypertrophy, or *hyperplasia*. The two forms of hypertrophy are thus comparable with the two forms of atrophy:—in simple hypertrophy as in simple atrophy, there is merely an alteration in the *size;* in numerical—an alteration in the *number* of the elements.

CHAPTER XI.

THE NEW FORMATIONS.

Increased nutritive activity of a tissue—as has been seen in the preceding chapter—leads not only to the enlargement of its component elements, but also to the production of new ones. It is this production of *new elements*, and the various structures to which they give rise, that constitutes the New Formations.

The New Formations comprise both *inflammatory* and *non-inflammatory* growths. Of these, the latter—which include the various kinds of tumours, together with some growths to which the term "tumour" is not strictly applicable—will be considered in the present part of this work, whereas the inflammatory growths will be treated of in the chapters on "Inflammation."

Tumours,—which constitute the greater portion of the non-inflammatory formations—are growths which, having attained a certain size, either remain permanent, or, more frequently, *tend continuously to increase.* In their development and growth they are characterized by their *independence* of the rest of the body; they increase in size by virtue of their own inherent activity, which differs from, and is independent of, that of the surrounding tissues.

There are, however, some non-inflammatory growths which cannot be regarded as "tumours" in the ordinary acceptation of that term. Amongst these are the *numerical hypertrophies* described in the preceding chapter, and *possibly* some of the *general* hyperplasias of the connective tissue of organs, as certain forms of cirrhosis. The characteristics of syphilitic growths again, and of cancerous infiltrations of organs, differ in some respects from what have been above described as those of tumours.

The inflammatory new formations differ from the non-inflammatory in being caused by some *irritation*, upon the removal of which the process of growth usually ceases. They are characterized by their *instability;* they either rapidly undergo retrogressive changes, or, at the most, form a tissue which in its structure and life is similar to that from which they originated. Their tendency is gradually to approximate to a healthy condition, and, not like that of the tumours, continuously to increase and deviate from the normal type.

Whatever be the nature of the new formation it is always the direct product of the elements of a pre-existing tissue, these elements being in some cases migrated white blood-corpuscles. In order therefore to understand the pathology of the new formations, it is necessary to be intimately acquainted with the histology and mode of development of the normal tissues.

ETIOLOGY OF THE NEW FORMATIONS.*—As the new formations are the result of the increased nutritive activity of the elements from which they originate, it will be readily understood that their causes must for the most part be obscure, and that in many cases all that can be said is, that the new growth is the result of the *spontaneous* activity of the elements from which it springs. Sometimes, however, the causes are either wholly or partially ascertainable. They may be divided into *constitutional predisposing*, and *direct exciting*, causes.

Constitutional Predisposing Causes.—That many growths owe their origin to some constitutional taint, has long been an universally accepted pathological doctrine.

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* This, together *with the* remainder of the present chapter, ap*plies only to the non-inflammatory* growths.

The constitutional cause has frequently been regarded as a general one, as consisting either in some alteration in the constitution of the blood, or in some abnormal condition of the physiological processes throughout the entire organism. It was formerly supposed that many new formations were the result of an exudation from the blood-vessels, and that the elements of the growth were produced spontaneously in the exuded structureless blastema. Such growths were looked upon as the local expression of a vitiated constitution of the blood,—a *dyscrasia.* Although this hypothesis is now universally abandoned, and all new formations are known to originate from pre-existing cellular elements, an alteration in the constitution of the blood or in the performance of the physiological processes throughout the body, is still regarded by many as playing an important part in their causation.

It is the malignant new formations which are thus supposed to owe their origin to the existence of a *general* constitutional taint. These growths are said to be of a *constitutional* origin, in contradistinction to the non-malignant growths which are looked upon as purely *local.* This hypothesis is principally based upon the clinical characteristics of the malignant growths—their tendency to recur after removal, their multiplicity, and the difficulty or impossibility of completely eradicating them.

It is said that the development of malignant growths is frequently preceded by an unhealthy state of the constitution—a cachexia. In the majority of cases of malignant formation, however, there is no evidence of any such cachexia preceding the local growth. The individual is usually in good health at the time of the occurrence of the primary tumour. The general impairment of nutrition and emaciation, which constitute the cachexia, are *secondary* to the local growths, and are in direct proportion to their *extent and situation*:—the more extended the local lesions, *the greater* the amount of discharge, the more the lymphatics and the digestive organs are involved, the more marked is the attendant cachexia.

The multiplicity of malignant growths is also adduced as an argument in favour of the existence of a general constitutional taint. The fact that malignant growths are frequently multiple, constitutes in itself no ground for such a conclusion. The multiplicity is for the most part a *secondary* phenomenon, the secondary tumours resulting from infection by the primary one. Simple *primary* multiplicity is not so characteristic of malignant as of many other tumours—the lipomata, fibromata, sebaceous tumours, and warts, are all more often *primarily* multiple than cancer. Multiplicity in many cases is evidence rather of a *local* than of a general taint. In scrofula, for example, the lymphatic glands generally are prone to become the seats of new growths, and tumours are often multiple in bone without occurring in other tissues. In such cases there would appear to be a *local* rather than a *general* cause.

The recurrence of the malignant growth after removal at the seat of the operation, may again be owing to the removal having been incomplete, some of the proliferating elements or of the growth itself having been left behind. The cellular elements of malignant tumours often extend into the adjacent tissues for some distance beyond the confines of the tumour, and as the physical characters of the infiltrated tissues differ in no way from those of the healthy, there are no means of certainly determining how far wide of the tumour the incision must be carried in order to include the whole of the affected structures. (See "Malignancy.") A tendency to local recurrence is a property possessed by many growths, and it can be explained on local grounds without the necessity of admitting the existence of a general taint.

Lastly, the fact that malignant growths are usually *followed by the development* of similar growths in the lymphatic glands and in internal organs, may in most cases be more readily explained—as will be seen when speaking of "malignancy"—by regarding these as the result of infection by the primary tumour, than by ascribing them to the existence of a common constitutional cause.

The reasons already adduced in a preceding chapter (see "Introduction"), for considering all changes in the constitution of the blood as secondary to local causes, would appear of themselves to be sufficient to render untenable the hypothesis of a *primary* blood dyscrasis. Any abnormal condition of the blood which may be associated with the development of malignant tumours must probably be regarded as resulting either from the absorption of deleterious substances, from the entrance into it of the elements of the growth, from the drain of an attendant discharge, or from interference with the processes of digestion, assimilation, or secretion, or with the formation of the blood itself. At the same time it must be borne in mind, when discussing the possibility of the development of malignant growths being the result of a "blood-disease," that the emigration of white blood-corpuscles may play some part in the process. How far this is the case, as will be seen hereafter, we are at present unable to determine. We know that this emigration constitutes a prominent feature in the process of inflammation, and if future researches should show that it also occurs in the development of malignant new formations whilst in those which are non-malignant it is entirely wanting, it would go far towards rendering the existence of a malignant dyscrasia beyond dispute. In the present position of our knowledge, however, in which it is *only probable* that an emigration of leucocytes may play some part in the development of all new growths, both innocent and malignant, any argument in favour of the existence of a blood-dyscrasia as the cause of the development of the latter based upon such considerations would be unjustifiable. If an emigration of leucocytes does take place, it is more in accordance with facts and with the general history of malignant growths to suppose the existence of some peculiarity in the tissues into which the elements escape which determines their special development.

Although there would thus appear to be no necessity to admit the existence of a general constitutional cause in order to explain the clinical characters which constitute malignancy, there can be no doubt that many growths, both innocent and malignant, have a constitutional origin. The possibility of the existence of such a constitutional cause must therefore be borne in mind in accounting for the development of secondary malignant growths, as although these may result from infection, they may also owe their origin to the same causes as those which induced the primary one. Whether the constitutional cause is a *general* one—consisting in some specific peculiarity of the entire organism, or whether it is *local* in its nature, and consists in some constitutional peculiarity of the tissues from which the new growths originate, some peculiarity which renders them more prone than other tissues to undergo abnormal development, is unknown; although the latter supposition seems to be the more probable one.

The influence of hereditary predisposition upon the occurrence of many growths, appears to point to the existence of a *local,* rather than to that of a *general* constitutional taint. In scrofula, for example, which is a markedly hereditary disease, the tendency of the lymphatic glands to undergo excessive development from very slight degrees of irritation, is probably to be regarded as owing to a predisposition of the glands themselves, and not to any *general* constitutional state. The same is probably true of many other constitutional tendencies. Nævi, tumours of the skin, uterus, mammæ, stomach, and of other parts, are again all unquestionably sometimes hereditary; and here also the tendency would appear to consist in a predisposition of the tissues themselves to become the seats of new formations.

The tendency sometimes observed in *particular* tissues to generate new formations, points again to a local cause. The osseous system, for example, may be the seat of new growths—tumours occurring in nearly all the bones, and not being met with in other parts. Tumours may in the same way be multiple in other tissues.

Direct Exciting Causes.—The existence of a direct exciting cause is more capable of demonstration than a constitutional one. It consists either in some direct irritation of a tissue, which is by this means stimulated to increased development, or in the migration or transmission of elements from some primary growth, which by proliferating in the tissues in which they lodge constitute the centres of secondary formations.

The direct irritation of a tissue may be owing to simple *mechanical* or *chemical*, or to *specific* irritants. Simple mechanical or chemical irritation can, however, under no circumstances be the *only* cause of the development of the growth. The effect of such irritations alone, is to cause an inflammatory formation; in order for them to produce a non-inflammatory one—a tumour, there must be some special predisposition of the tissue itself:—the irritation can merely *determine* its development. The influence of simple irritation in the production of new formations is exemplified by the frequent occurrence of epithelioma on the lips of smokers, from the irritation of the pipe; and on the penis and scrotum of chimney-sweepers, from the irritation of the soot ("chimney-sweep's cancer"). The numerous recorded instances of the development of a tumour following some external violence or injury, leave little doubt that these also sometimes stand to one another in the relation of cause and effect. Lastly, it is those organs which are most exposed to irritation from external causes, as the stomach, the uterus, the mammary-gland, and the rectum, which are especially liable to become the seats of new growths.

In other cases the irritant is *specific*, and induces specific changes in the tissues. It may either be introduced from without, or originate from some morbid product within the body. As to its nature—it is probably in most cases matter in a state of extremely fine division, and not in a state of solution. Such specific irritants can only act upon the tissues through the medium of the blood, lymph, or nutritive fluids. The dissemination of cancer and of other malignant growths is possibly thus partly owing to the transmission of particles of the growth, which cause the tissues with which they come in contact to generate similar formations. Here also, however, there may exist some special predisposition of the tissues themselves.

The development of new formations from cellular elements which have either migrated or been conveyed from their original habitat, constitutes the most frequent and important mode by which secondary malignant growths originate. The elements, which may either migrate spontaneously from the primary growth or be carried by the blood or lymph streams, proliferate in the tissue in which they lodge, and so develop into secondary formations. It is possible also that by their mere *contact* with the adjacent elements, they may induce in these similar development. This mode of origin of new formations is exemplified by the history of many malignant growths, and by this means these are most frequently disseminated. It will be more fully described when speaking of "Malignancy."

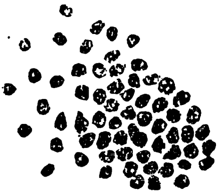
DEVELOPMENT.—In studying the development of the new formations, it is important, in the first place, to bear in mind what has been already stated—that they are in all cases the direct product of pre-existing cellular elements. In their development they also resemble the normal tissues:—every pathological growth has its physiological prototype.

The elements from which new growths most frequently originate are those belonging to the *common connective tissue*, and to the blood-vessels and lymphatic system with which it is so intimately associated. By common connective tissue is meant that tissue which in all parts surrounds the blood-vessels, and is so universally distributed throughout the entire organism. This must be carefully distinguished from the formed connective substances—tendon, cartilage, bone, &c. In this common connective tissue we distinguish two kinds of cells—the stable cells (connective tissue corpuscles), and the mobile cells, which are probably wandering white blood-corpuscles. These cells are in intimate relation with the endothelium of the lymphatics, the latter vessels commencing as serous canals which are universally distributed in the tissue. Further, both the endothelium of the lymphatics and that of the blood-vessels closely resemble in their physiological functions the fixed cells of the connective tissue.

In the process of development of new growths from this common connective tissue, the part which is played by the different cellular elements cannot in our present state of knowledge be certainly stated. It is, however, in the highest degree probable that it is the mobile cells which are principally concerned. These cells are the most active, and consequently the most capable of multiplying by division. It is equally probable that the number of these mobile cells is materially increased by an abundant emigration of white blood-corpuscles from the vessels. Respecting the fixed connective tissue cells and the endothelium of the blood-vessels and lymphatics—it must be admitted that these, although inferior in their formative powers, also undergo active changes and divide, and thus increase the number of the newly-formed elements. In all cases the division and multiplication of the cells is accompanied by an increase of their protoplasm; and in those which contain nuclei, the division of the nucleus usually precedes that of the cell (see "Genesis of Cells").

Whatever be the part played by the respective elements in the process of development of the new growth, the first result of their combined activity is to produce a new tissue, composed of innumerable small roundish-shaped cells, from $\frac{1}{1800}$ to $\frac{1}{2500}$ of an inch in diameter, often enclosing a large, round, ill-defined nucleus, which usually only becomes visible after the addition of water or of acetic acid. These cells, which are usually known as *indifferent* cells, possess no limiting membrane, but consist of little masses of protoplasm which are almost in close contact with one another. (Fig. 23.) They are indistinguishable from the cells of a granulation, and from many of those met with in the rapidly-growing connective tissue of the embryo. In some cases the protoplasm continues to increase and the nuclei to divide without any subsequent division of the cell taking place, and thus are produced large irregular-shaped masses of protoplasm containing numerous nuclei. These are the giant or myeloid cells which are met with in the medulla of young bone and in many sarcomatous tumours (see "Myeloid Sarcoma," Fig. 29). Thus the first stage in the process of development consists in the formation of an embryonic tissue, and this embryonic tissue subsequently develops into the tissue *of which the new growth* is composed. It is often im-

FIG. 23.



Embryonic ("*Indifferent*") *Tissue from the Edge of a Sarcomatous Tumour.* × 350.

possible to determine in this early stage of the growth what it will ultimately become—whether a fibroma, a sarcoma, or an enchondroma, &c.

The second stage of the process consists in the development of this embryonic ("indifferent") tissue into the tissue of the permanent growth, and this subsequent development closely resembles that of the immature connective tissue of the embryo. As from the immature connective tissue of the embryo are developed various connective tissue substances—fibrous tissue, mucous tissue, cartilage, bone, &c.—so may this embryonic connective tissue which constitutes the earliest stage of so many of the pathological new formations, become developed into various tissues, all of which more or less resemble the several varieties of the physiological connective tissues. The whole of the primary cells may form the same kind of tissue, in which case the growth will possess the same characters throughout; or it may be complex, some cells forming one kind of tissue and some another. A combination of two or more kinds of structure may thus be met with in the same tumour—as a combination of sarcoma and lipoma, of enchondroma and myxoma, and so on. What determines the ultimate development of the young cells, why they produce such various forms of growths, is as far from our knowledge as what determines the ultimate destination of the cells in the embryo.

Next to common connective tissue, the *epithelia*, surface and glandular, are the elements from which new formations most frequently originate; and as from connective tissue are produced growths of the connective tissue type, so do the growths originating from the epithelia resemble epithelium. Respecting the mode by which new growths are developed from epithelium—whether they are solely the offspring of pre-existing epithelial elements—we are unable to speak with certainty. The answer to this question must await a more certain knowledge of the way in which the epithelial structures normally grow and repair themselves. It appears probable that the normal production of epithelium is not entirely the result of the multiplication of epithelial cells, but that the mobile cells of the connective tissue by *contact* with epithelial elements may become developed into epithelium. It must, consequently, be admitted, at all events as equally probable, that pathological new formations which originate in connexion with epithelium may be in part the product of mobile elements belonging to the connective tissue.

From the remaining tissues, *muscle* and *nerve*, the development of new growths is comparatively rare, and in nerve-tissue it is even doubtful if formative processes ever occur.

According to the similarity or difference which subsists between the new growth and the tissue from which it grows, new formations are divisible into two classes—*homologous* and *heterologous*. When the growth resembles in its structure and development the tissue from which it originates, it is said to be *homologous*; when it differs it is said to be *heterologous*. A cartilaginous tumour, for example, growing from cartilage, is homologous, but growing from any other tissue, as from the parotid gland, it is heterologous. The same variety of tumour may thus be in one case homologous, in another heterologous. A purely homologous growth is therefore simply a *hyperplasia*—an excessive growth of a tissue in some particular part; any deviation from the type of the parent tissue constitutes heterology.

Heterology, however, is not limited to the production of a tissue which is dissimilar from that from which it originates; a growth is also said to be heterologous when it differs from the tissue in which it is *situated*, and this may occur without its being the direct product of the latter. It is heterology in this sense that is so *characteristic of the cancers*. These, which originate from epithelium, become heterologous owing to the growth and extension of the epithelium beyond its normal limits (see "Epithelioma"). The same form of heterology obtains in the case of growths originating from elements which have migrated or been carried from their original habitat, and have developed into a tissue which differs from that in which they are situated.

Heterology is often an evidence of malignancy. Many heterologous growths, however, are not malignant; slight deviations from the normal type are no evidence of malignancy. A purely homologous growth is never malignant. A growth primarily homologous may subsequently become heterologous; this is often seen when a long-standing innocent tumour suddenly exhibits malignant characters. A knowledge of the homology or heterology of a growth is therefore an important element in the determination of its innocent or malignant nature.

RELATION OF THE GROWTH TO THE SURROUNDING TISSUES.—The relation of the tumour to the surrounding structures will depend upon its mode of growth. Growth may take place simply by the continuous proliferation of the cells of which the tumour is composed. In this case it will merely displace the surrounding parts, and having attained a certain degree of development, a fibrous capsule is often formed around it, by which it becomes completely isolated. The lipomata, fibromata, and enchondromata are usually thus encapsuled. In other cases, growth takes place also at the circumference, by the continuous proliferation of the parent tissue. There is then no line of demarcation between the tumour and the matrix from which it grows, so that although to the naked eye it may appear separate, the microscope will discover in the adjacent tissues elements of the new growth. This is very common in the sarcomata and in *the cancers*, and is a common cause of local recurrence *after removal*. Lastly, the tumour may increase not only by the proliferation of its matrix, but also by invading other structures:—this occurs in those growths which are the most malignant (see "Malignancy").

Retrogressive Changes.—The development of the growth being complete, it becomes sooner or later the seat of retrogressive changes. The time at which these commence, varies:—as a rule the permanence and durability of a tumour bear an inverse relation to the rapidity of its growth, and to the inferiority of its organization. The more rapid the growth, and the more lowly organized the tissue formed, the less its durability and the sooner do retrogressive changes occur. The cancers and sarcomata, for example, which develope rapidly and consist for the most part of cells, quickly degenerate; their elements are unstable and soon perish. Osseous tumours, on the other hand, which develop more slowly, and consist of a more highly organized tissue, have a much greater stability, and are but little liable to retrogressive metamorphosis.

The retrogressive changes are similar to those met with in the physiological tissues. Impairment of vitality is followed by fatty degeneration and its various terminations — softening, caseation, and calcification. Pigmentary, colloid, and mucoid degeneration may also occur. New formations may also become the seats of an inflammatory process.

Malignancy.—By "malignancy" is understood the property possessed by many tumours of reproducing themselves either locally after removal, or in distant tissues. It is important not to confound the terms "malignancy" and "cancerous." "*Malignancy*" is a purely clinical term, and although in a high degree the property of the cancers, is by no means confined to them; the sarcomata, for example, being in many cases equally, or even more malignant. The term "cancer," *on the other hand, is* used to imply a definite structure, and as such is applied to a certain class of new formations.

The malignant properties of a tumour may manifest themselves either in the tissues immediately adjacent to it or in its neighbourhood, in the nearest chain of lymphatic glands, or in more distant parts. Some growths possess these properties in a higher degree than others, so that there are different degrees of malignancy. In many cases the malignancy of a tumour is so far limited that it gives rise merely to a local reproduction after removal. Such tumours have been separately classified by many surgeons as "recurrent" tumours. In other growths this tendency to local reproduction is associated with the development of similar growths in the nearest lymphatic glands; whilst in a third class of cases, to one or both of these conditions is added the reproduction of the growth in more distant tissues, especially in the lungs and liver. It will be advisable to treat of these three degrees of malignancy separately.

1. *Reproduction of the Growth in the Adjacent Structures.*—This is usually the earliest evidence of malignancy in a growth, and gives rise to its persistent recurrence *in loco* after removal by the surgeon. This tendency to the local reproduction of the tumour is principally owing to its mode of growth. The cellular elements of the tumour extend for some distance into the surrounding tissues, so that unless in the operation for its removal the incision be carried for some distance beyond the *apparent* confines of the growth, some of the elements may be left behind and thus constitute the centres of secondary formations. Such tumours therefore are not usually encapsuled, but extend by peripheral growth. In some cases, however, tumours which possess a distinct capsule may in the same way infiltrate the surrounding structures. The infiltration of the adjacent tissues by the elements of the tumour sometimes gives

rise, not only to the continuous enlargement of the primary growth, but also to the development of separate secondary growths in the immediate vicinity of the primary one. Whilst it must be admitted that the reproduction of a malignant tumour in the adjacent tissues is thus in most cases to be ascribed to the infiltration of the latter with its cellular elements, it is possible that the nutrient fluids of the tumour may by their influence upon the surrounding tissues be in part the cause of the abnormal development.

2. *Reproduction of the Growth in the nearest Lymphatic Glands.*—This is owing to the transmission by the lymph-stream of substances (probably cellular elements) derived from the malignant growth, which become arrested in the nearest lymphatic glands, and there cause the development of secondary formations. These are in all cases of the same nature as the primary tumour. When the lymphatic glands have themselves developed into secondary growths, they in their turn constitute new centres of infection, and may thus infect more distant glands or the immediately adjacent tissues. The tendency to reproduction in the lymphatic glands varies very much in the different varieties of malignant growths, being, for example, very marked in the cancers, whereas in the sarcomata it is comparatively rare. The reasons for these differences will be seen in the subsequent chapters.

3. *Reproduction of the Growth in Distant Tissues.*—This is usually the terminal process in the history of malignant growths. The reproduction of the malignant growth in distant tissues is in the great majority of cases owing to the entry of its elements into the blood-stream. The secondary growths, as in the lymphatic glands, are in all cases of the same nature as the primary tumour. They occur as a rule in those organs through which the blood from the primary tumour first passes—that is, in

those organs which present the first set of capillaries for the arrest of the transmitted materials. In malignant diseases of those organs, for example, which return their blood through the portal vein, as the stomach and mesenteric glands, it is the liver in which the secondary growths usually first occur, and when this has become involved, it may constitute a secondary centre of infection and in the same way cause tertiary growths in the lungs. Although this sequence is the rule, there are numerous exceptions. In some cases the organs which are nearest in the course of the circulation to the primary growth escape, whilst those more distant become affected. This may be owing to one organ being more predisposed to the influence of the infecting materials than another; or to the capillaries of the proximal organ allowing particles to pass through them, whereas those of the more distant one are small enough to arrest them. Lastly, it must be borne in mind, that the secondary growths may be entirely independent of the primary one, their origin being due to the same cause.

Although the general dissemination of a malignant growth is thus in most cases owing to the transmission of its elements by the blood-stream, this is not the only way in which it may be brought about. Exceptional cases have been described in which the elements of a tumour have been distributed and caused secondary growths in other ways—as by passing down the trachea, between the layers of the peritoneum, &c.

The evidences of malignancy in a growth thus consist—in its invasion of the surrounding structures, the implication of the neighbouring lymphatics, and the occurrence of similar growths in internal organs. As a general rule it may be stated that the more juice a growth contains, and the richer it is in blood-vessels and lymphatics, the more quickly will it infect the lymphatic glands, and internal organs; on the other hand, the poorer it is in blood-vessels and lymphatics, the more are its infecting properties confined to the neighbouring tissues.

The determination of the innocent or malignant nature of any growth will principally depend upon its microscopical characters, and, as will be seen when considering the various kinds of tumours, the differences which exist in their clinical characters are in great measure to be explained by differences in their position, minute structure, and mode of growth. Many varieties of new formations are invariably malignant, as the cancers and sarcomata; hence any growth which from its minute structure must be included under these heads, must be regarded as being of a malignant nature.

Classification.—New formations may be classified upon an anatomical, a physiological, or a clinical basis. Although a physiological and clinical classification are much to be desired, in the present state of our knowledge they must be very incomplete. A classification of the new formations according to their histological characters is consequently here adopted. Such a classification may be most advantageously made in accordance with the classification of the physiological tissues:—

CLASSIFICATION OF THE NEW FORMATIONS.

Type of the Connective Tissues.

Type of embryonic connective tissue	Sarcoma.	
„ fibrous tissue	Fibroma	
„ mucous tissue	Myxoma.	
„ adipose tissue	Lipoma.	
„ cartilage	Enchondroma.	
„ bone	Osteoma.	
„ lymphatic tissue	The Lymphomata	Simple Lymphoma. Lymphadenoma Leukæmia.

Type of the Epithelial Tissues.

Papilloma.
Adenoma.
The Carcinomata
- Scirrhus.
- Encephaloid.
- Colloid.
- Epithelioma.

Type of the Higher Tissues.

Type of muscle	Myoma.
„ nerve	Neuroma.
„ blood-vessels	Angioma.

CHAPTER XII.

THE SARCOMATA.

THE sarcomata are tumours consisting of embryonic connective tissue. Of these there are several varieties, depending upon the size and configuration of the cells, and the nature of the intercellular substance. They include what have generally been known in this country as *fibro-plastic*, *fibro-nucleated*, *recurrent-fibroid*, and *myeloid* tumours.

Connective tissue in its embryonic condition is an immature tissue in a state of rapid development. In its most immature state it differs from the fully developed tissue in consisting almost entirely of small round cells, whilst its intercellular substance, instead of being fibrous, is soft and amorphous. This is the common condition of connective tissue in the primary stages of all rapid formative processes, as already described when speaking of it as the tissue from which many tumours of the connective-tissue class originate (see "Development of New Formations").

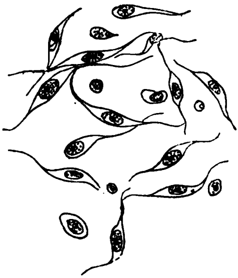
In the process of development of this embryonic into mature connective tissue, the cells diminish in number, many of them assume a spindle shape, and the intercellular substance fibrillates. Similar changes are seen in inflammatory conditions of connective tissue. Here also many of the small round cells which constitute the "granulation-tissue" become spindle cells, and the granulation tissue ultimately develops into the fibrous tissue of the cicatrix. In the sarcomata, however, the connective tissue retains the embryonic state throughout its growth; there is a progressive formation of embryonic tissue; and although the small round cells commonly reach a higher stage of development and become spindle-shaped, development rarely proceeds to the formation of a completely fibrillated structure.

STRUCTURE.—The sarcomata may thus be defined as tumours consisting of connective tissue which throughout its growth retains the embryonic type. The *cells*, which constitute nearly the whole of the growth, consist for the most part of masses of nucleated protoplasm, and rarely possess a distinct limiting membrane. They present many variations in size and form; as a rule, however, they preserve the same general characters in the same tumour. There are three principal varieties—the *round*, the *fusiform*, and the *myeloid* cells.

The *round* cells are many of them indistinguishable from lymphatic cells or white blood-corpuscles. Others are somewhat larger and contain an indistinct nucleus with one or more bright nucleoli: these more closely resemble the cells of a granulation.

The *fusiform*, or *spindle-shaped* cells, are the so-called "fibro-plastic cells" (Fig. 24). They are long narrow cells, terminating at each end in a fine prolongation. Some of them may be broader, approaching the epithelial type; others more or less stellate. They are sometimes slightly granular, and they enclose a long oval nucleus, with or without nucleoli. In size they vary considerably.

FIG. 24.



Cells from a Spindle-celled Sarcoma. × 200.

These cells represent a higher state of development than the round cells, resembling those met with in embryonic tissue which is in the process of forming mature connective tissue. (See Fig. 63 B.)

The *myeloid*, or *mother* cells, are much larger than either of the preceding, and are analogous to the cells met with in the medulla of fœtal bone. (See Fig. 29.) They are large irregular-shaped masses of nucleated protoplasm, for the most part more or less spherical, and often possessing numerous offshoots. They are finely granular, and contain several round or roundly-oval nuclei, each with one or more bright nucleoli. The nuclei may be exceedingly numerous, one cell containing as many as thirty. Both the cells and nuclei vary considerably in size.

An *intercellular substance* exists in all the sarcomata, although it is usually very small in quantity, the cells lying in nearly close apposition. It may be perfectly fluid and homogeneous, or firmer and granular, or more or less fibrillated. Chemically it yields albumen, gelatin, or mucin.

The *blood-vessels* are very numerous, and are either in direct contact with the cells, or separated from them by a little fibrillated tissue. Their distribution is very irregular, and their walls often consist of embryonic tissue similar to that of the growth which they supply; hence the frequency with which rupture and extravasation of blood take place.

DEVELOPMENT.—The sarcomata always originate from connective tissue—either from the subcutaneous, the submucous, or the subserous tissues, the fasciæ, the connective tissue of organs, the periosteum, or the medullary tissue of bones. Their growth may take place in two ways, by the multiplication of their own elements—*central* growth, and by the continuous invasion of their matrix—*peripheral* growth. A peripheral growth is the great characteristic of the sarcomata; they usually increase by the continuous invasion of their connective-tissue matrix, so that no line of demarcation exists between the two. They frequently also invade other tissues, the elements of the growth extending for some distance into the surrounding structures. This infiltrating tendency of the sarcomata varies considerably in the different varieties, being much more marked in the round-celled than in the spindle-celled and myeloid growths. A purely central growth is less common. A sarcomatous tumour, however, often becomes encapsuled and growth takes place within the capsule; but even in this case the capsule is sometimes merely that of the part within which the growth originates, as the periosteum, or the capsule of a lymphatic gland.

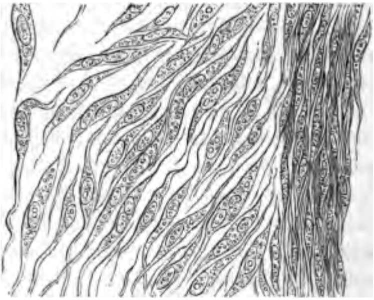
SECONDARY CHANGES.—The most important of these is fatty degeneration. This always occurs to a greater or less extent in the older portions of the growth, causing softening, caseation, or the production of cyst-like cavities. It is frequently associated with destruction of the blood-vessels and hæmorrhage: the latter may give rise to pigmentation, and the formation of sanguineous cysts. Calcification, ossification, and mucoid degeneration are less common. The occurrence of calcification, ossification, and pigmentation is influenced by the predisposition of the matrix from which the growth is produced:—thus calcification and ossification are more prone to occur in tumours originating in connexion with bone, pigmentation in those originating from the cutis or eyeball.

VARIETIES.—Although all the sarcomata possess the same general characters, they present many histological and clinical differences which may serve as bases for their classification. The occurrence of the various secondary changes—ossification, pigmentation, mucoid degeneration, and the formation of cysts, impart their respective characters to the growth; hence *osteoid-sarcoma*, *melanotic-sarcoma*, and *cystic-sarcoma*, have been described as distinct varieties. This is to a certain extent justifiable, inasmuch as sarcomata which have undergone these transformations, in many cases possess the property of reproducing the same characters when they occur secondarily in other parts. Then, again, sarcomatous tumours are sometimes complex in their structure, and are associated with other tissues belonging to the connective-tissue group. A combination of sarcoma with fatty, cartilaginous, and osseous tissue, is thus not uncommonly met with. This is owing to the embryonic tissue exhibiting a tendency to develop into the different varieties of connective tissue. (See "The New Formations.") The following histological classification, based upon the three different forms of cells already described, is perhaps the most convenient. It must, however, be borne in mind, that all the varieties of cells may be found in the same tumour, although the majority are usually of the same type; hence, the *majority* will determine the class to which the growth belongs.

SPINDLE-CELLED SARCOMA.

This, which includes the growths long known in this country as "fibro-plastic," "recurrent fibroid," &c., is the most common of all the sarcomata. It is more closely allied to the fibromata than are the other varieties of sarcoma, inasmuch as it consists of a tissue which must be regarded as occupying an intermediate place between embryonic and fully-developed connective tissue. It consists of spindle-shaped and fusiform cells, varying considerably in size, and nearly in close contact, there being very little intercellular substance. (Fig. 25.) The cells, which contain well-marked oval nuclei, are parallel to one another, and are arranged in bundles which pass in all directions through the growth, so that on section it presents a somewhat fasciculated appearance. In some parts there may be partial fibrillation. The spindle-celled sarcomata grow from the periosteum, the fasciæ, and from connective tissue in other parts. They are often encapsuled, much more frequently so than the round-celled growths, but they usually extend by peripheral growth, and sometimes infiltrate the surrounding structures.

FIG. 25.

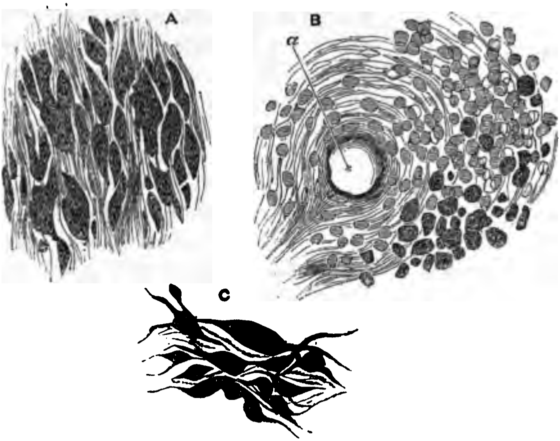


Spindle-celled Sarcoma. To the left—the cells have been separated by teasing, so that their individual forms are apparent; to the right—they are in their natural state of apposition, such as would be seen in a thin section of the tumour. × 350 (Virchow.)

MELANOTIC SARCOMA.—This is a variety of sarcoma in which many of the cells contain granules of dark-coloured pigment. By far the greater number of melanotic tumours are sarcomata, and most of the growths which were formerly described as "melanotic cancers," belong in reality to this class of new formations. Not only are these melanotic tumours most frequently sarcomata, but the majority of them consist of spindle-shaped cells—hence they are described in the present section.

The melanotic sarcomata originate principally in two situations—in the choroid coat of the eye, and in the superficial integuments. In both of these situations pigment is a normal constituent of the tissues, and this tendency of structures normally containing pigment to originate melanotic growths, is exceedingly characteristic. (See "Pigmentary Degeneration.") These tumours usually consist of spindle-shaped cells, although in some cases the prevailing type of their elements is round or oval. (Fig. 26.) The pigment, which gives to them their distinctive characters, consists of granules of a brownish or dark sepia colour, which are distributed within the cells. (Fig. 26 c.) Frequently, only a very small proportion of the cells are pigmented, whilst in other tumours the pigmentation is much more universal; in all

FIG. 26.



A Melanotic Sarcoma of the Penis.

A.—A thin section, showing the general arrangement of the elements. × 200.

B.—A section from the peripheral part of the growth, showing the "indifferent cells," amongst which are small isolated pigmented elements. At *a*, a blood-vessel is seen. × 200.

C.—Some of the elements separated by teasing. In these the pigment-granules are well seen. × 400.

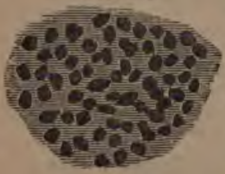
cases, however, a large number of the elements will be found to be quite free from pigment.

These melanotic tumours are amongst the most malignant of the sarcomatous growths. They reproduce themselves often very rapidly in distant tissues, and in doing so, although they almost invariably maintain their melanotic characters, the degree of the pigmentation of the secondary tumours varies considerably; whilst many of them may be perfectly black in colour, others may be much paler, and perhaps only partially streaked with pigment. The secondary growths may occur in almost every organ of the body—the liver, the spleen, the kidneys, the lungs, the heart, and also the lymphatic glands and subcutaneous tissue, may all be simultaneously involved. The author has observed, that when occurring in internal organs, the pigmentation is not always limited to the secondary nodules, but that many of the cells proper to the organ itself are filled with granules of similar pigment, which is most abundant in those cells which are immediately adjacent to the new growth. This pigmentation of the cells of the organ often extends for some distance beyond the confines of the tumour.

ROUND-CELLED SARCOMA.

This is of softer consistence than the preceding, and from its frequent resemblance in physical characters to encephaloid, is sometimes known as "medullary," "encephaloid," or "soft" sarcoma. Histologically, it is elementary embryonic tissue, consisting of the round cells already described, embedded in a scanty, and usually soft, homogeneous,

FIG. 27.



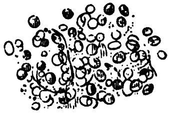
Round-celled Sarcoma. A thin section of a small round-celled sarcoma of the liver. × 200.

or finely granular intercellular substance. (Fig. 27.) The cells usually resemble those met with in the most elementary embryonic tissue; less frequently, they are larger, and contain large round or oval nuclei, with bright nucleoli. There is an almost complete absence of fusiform cells, and of the partial fibrillation which is so frequent in the more highly developed spindle-celled variety.

The round-celled sarcomata are of a uniform soft brain-like consistence, and of a somewhat translucent greyish or reddish-white colour. On scraping the cut surface, they yield a juice which is rich in cells. They are exceedingly vascular, the vessels often being dilated and varicose, and from their liability to rupture, they frequently give rise to ecchymoses and to the formation of sanguineous cysts. They grow from the cutis, the subcutaneous cellular tissue, the periosteum, the fasciæ, and from the connective tissue of organs. They extend rapidly by peripheral growth, and infiltrate the surrounding structures. From their clinical and physical characters, these tumours are very liable to be confounded with encephaloid cancer:—they are distinguished by the absence of an alveolar stroma, and by the uniformity in the character of their cells.

GLIOMA.—This is a variety of round-celled sarcoma growing from the neuroglia or connective tissue of nerve. It consists of very small round cells, embedded in an exceedingly scanty, homogeneous, granular, or slightly fibrillated intercellular substance. (Fig. 28.) Some of the cells may possess fine prolongations which, by communicating with one another, form a somewhat reticulated structure. These tumours occur in the grey and white substance of the brain, in the cranial nerves, and in the retina. The retina is much their most

FIG. 28.



Glioma. A thin section of a glioma of the cerebellum. × 200.

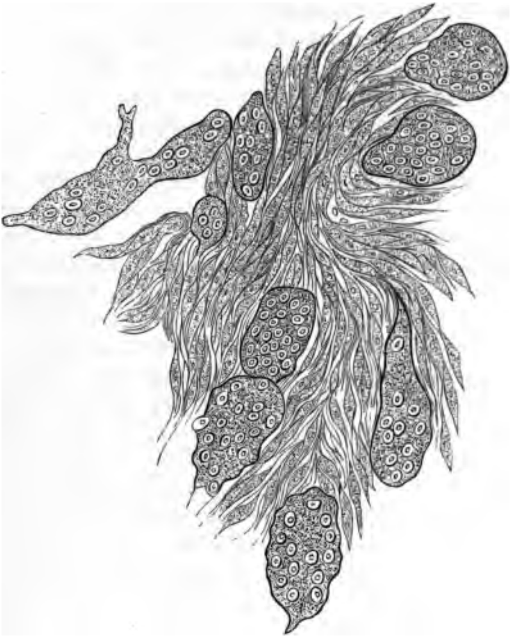
frequent seat. They usually commence here as a minute nodule, which may gradually increase until it projects as a large fungating tumour from the orbit. They are not encapsuled, and although they may infiltrate the tissues in which they lie and cause secondary growths in their vicinity, they very rarely reproduce themselves in the lymphatic glands or in internal organs. Glioma is almost exclusively a disease of childhood.

MYELOID SARCOMA.

This, which is the well-known *myeloid* tumour, is closely allied to the spindle-celled growths. It possesses, however, certain histological peculiarities depending upon the characters of the tissue from which it grows. Myeloid tumours always occur in connexion with bone, and frequently originate in the medullary cavity. They consist of the large, many-nucleated cells already described as "myeloid cells,"—which resemble the cells of the medulla in a state of excessive nutritive activity—together with numerous fusiform cells like those met with in the spindle-celled varieties. There are also some smaller round and oval elements. The large myeloid cells, which give to these tumours their distinctive character, are usually much more numerous in those growths which originate in the medullary cavity than in those which spring from the periosteum. These various forms of cells are nearly in close contact, there being very little intercellular substance. (Fig. 29.)

Myeloid tumours always grow in connexion with bone, the heads of the long bones being their favourite seat. They are also very frequently met with springing from the periosteum of the upper and lower jaws, where they are usually known as *epulis*. When originating within the medullary cavity, the compact tissue of the bone becomes expanded over them, and they thus often communicate on palpation the peculiar sensation known as "egg-shell crackling." In some cases they are exceedingly vascular and give rise to distinct pulsation, and even to the generation of an aneurismal murmur: this is most frequent in those of the lower extremity. These tumours are of firmer consistence than the other varieties of sarcoma; many of them are firm and fleshy, others are softer, more resembling size-gelatin. They are not pulpy and grumous like the soft sarcomata, neither do they

FIG. 29.



Myeloid Sarcoma. (Virchow.)

present the fasciculated appearance of the spindle-celled varieties. Their cut surface has an uniform succulent appearance, often mottled with patches of red. They are often encapsuled by the periosteal covering of the bone from which they grow.

CLINICAL CHARACTERS OF THE SARCOMATA.—The sarcomata occur most frequently in early and middle life, and they are amongst the most malignant of the new formations. They are especially characterized by their great tendency to extend locally and to infiltrate the surrounding structures, so that they are exceedingly prone to recur *in loco* after removal. They rarely infect the lymphatic glands, and in this respect present a marked contrast to the cancers. They are also very liable to become generally disseminated, although this is not usual in the earlier stages of the disease. The secondary growths occur most frequently in the lungs. The dissemination is effected by means of the blood, and this is owing to the thinness of the walls of their blood-vessels and to the immediate contact of these with the cells of the growth—conditions most favourable to the entrance of the cellular elements into the circulation. The dissemination of the sarcomata is, on this account, sometimes more rapid than that of the cancers. In the latter, extension in the early stage takes place principally by the lymphatics, and dissemination by the blood only occurs in the later stages of the disease. The secondary sarcomata usually resemble the primary one, but in exceptional cases the several varieties may replace one another.

These malignant characters are possessed by the different varieties of sarcoma in different degrees. As a rule, the softer and more vascular the tumour, and the less its tendency to form a fully-developed tissue, the greater is its malignancy. The soft, round-celled varieties are thus usually much more malignant than the firmer spindle-celled growths. Their infiltrating powers are much greater, they sometimes infect the lymphatic glands (which is exceedingly rare in the spindle-celled growths), and they tend to reproduce themselves very rapidly in internal organs. This is probably partly owing to the small round cells being endowed with greater powers of spontaneous movement than the spindle-shaped and larger cells; hence they more readily make their way amongst the tissues and into the blood-vessels. Amongst the spindle-celled tumours the degree of malignancy varies considerably. As a rule largeness of the spindle elements and the existence in many of them of more than one nucleus, is an evidence of special malignancy. Then, again, the presence of a distinct capsule limiting the growth must be taken into account in judging of the degree of its malignancy. The myeloid growths are perhaps the least malignant, they may however also give rise to secondary growths in internal organs.

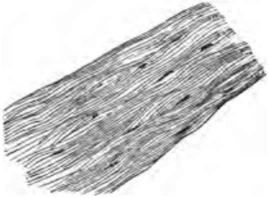
CHAPTER XIII.

THE FIBROMATA.

THE fibromata, fibrous, or connective-tissue tumours, are tumours consisting of fibrous tissue.

STRUCTURE.—In structure the fibromata present the same variations as those met with in fibrous tissue. Some of them are composed of firm, dense, fibrous tissue, such as constitutes tendons; others are laxer and less fibrous in consistence, more resembling the connective tissue of the cutis. The fibres (Fig. 30), which constitute the chief part of the growth, are closely interlaced, and are distributed without any definite arrangement, or grouped in bundles of various sizes: they are frequently arranged concentrically around the blood-vessels. The cells, or as they are usually called, the connective-tissue corpuscles, are very few in number, and usually only become visible after the addition of acetic acid. They are minute, spindle-shaped, fusiform, or stellate bodies, the latter having processes of varying length which communicate with similar processes from neighbouring cells. They contain in some cases an oval nucleus. The size and number of these cells varies with

FIG. 30.



Fibrous Tumour. × 200.

the rapidity of growth—the slower the growth the more fibrous the tissue, and the smaller and less numerous are the cells.

The fibromata usually contain but very few blood-vessels. In some cases, however, these are more numerous, and form a cavernous network, the walls of which are firmly united to the tissue of the tumour so that when divided or ruptured, they are unable to retract. In such cases, injury to the tumour is often followed by profuse hæmorrhage.

DEVELOPMENT.—The fibromata always originate from connective tissue, either from the cutis or subcutaneous connective tissue, from the submucous or subserous tissue, from fasciæ, the periosteum, the neurilemma, or from the connective tissue of organs. In the earliest stages of their growth they consist of embryonic tissue, the cells being very numerous, and the intercellular substance soft and amorphous (see "Development of New Formations"). The latter, however, subsequently fibrillates, the cells diminish in number, many of them become spindle-shaped, and the embryonic becomes fully developed connective tissue. The slower the process of development, the less marked are these embryonic characters. The fibromata are almost always limited by a fibrous capsule, which separates them from the surrounding structures. Their growth is slow and central, taking place within the capsule.

SECONDARY CHANGES.—Of these, partial mucoid softening and calcification are the most common. Ulceration also sometimes occurs in those growths which are situated in the submucous tissue.

VARIETIES.—Fibrous tumours present some variations in their characters, which depend for the most part upon the tissues from which they grow. Those growing from the cutis are *softer and* less dense in consistence than *those met with in many* other situations; they usually also have papillæ on their surface. These growths from the cutis are by no means uncommon, and may form enormous tumours. They are frequently multiple, and in their growth often become pedunculated. They commonly occur in middle or advanced life.

Another variety of fibrous tumour grows in connexion with nerves, and is often described as *neuroma*. True neuromata, however—*i.e.*, new formations of nerve-tissue—are amongst the rarest forms of new formations. These fibrous growths most frequently occur in connexion with the superficial nerves. They grow from the neurilemma, and as they increase in size the nerve-fibres become expanded over them, so that they often cause considerable pain—hence the term "painful subcutaneous tubercle" which is sometimes applied to them.

The fibroid tumours of the uterus, which are often regarded as fibrous tumours, appear in most cases to be overgrowths of the involuntary muscular tissue of the organ. They will therefore be described with the muscular tumours. (See "Myoma.")

PHYSICAL CHARACTERS, &c.—Fibrous tumours are usually more or less spherical or oval in shape, and are frequently lobulated on the surface. Their consistence varies:—they may be exceedingly firm, dense, and fibrous, or softer and more succulent. On section, they usually present a greyish-white basis substance, intersected with opaque white glistening fibres. They are generally single, except when growing from the neurilemma or cutis, in which situations they are frequently multiple.

CLINICAL CHARACTERS.—Clinically the fibromata are perfectly innocent, and have little or no tendency to recur locally after removal.

CHAPTER XIV.

THE MYXOMATA.

THE myxomata are tumours consisting of mucous tissue. Mucous tissue is a translucent and succulent connective tissue, the intercellular substance of which yields mucin. Physiologically, this tissue is met with in two forms, and in two situations:—one—in the vitreous humour of the eye, in which the cells are roundish and isolated; the other —in the umbilical cord, in which the cells are fusiform or stellate and give off fine trabeculæ which anastomose with one another. In both, the intercellular substance is homogeneous and yields mucin. The connective tissues generally in their embryonic condition, as already stated when describing "mucoid degeneration," possess an intercellular substance containing large quantities of mucin. New formations may undergo a mucoid change, and thus closely resemble in their physical and chemical characters the myxomata. A myxoma, however, is a growth which consists of mucous tissue. The myxomata are thus very closely allied to the sarcomata, and by many are included in the same class of new formations.

STRUCTURE.—The cells present the two varieties met with in the physiological tissues. The majority are angular and stellate, with long anastomosing prolongations and trabeculæ. (Fig. 31.) Others are isolated, and fusiform, *oval, or spherical in* shape. They usually possess

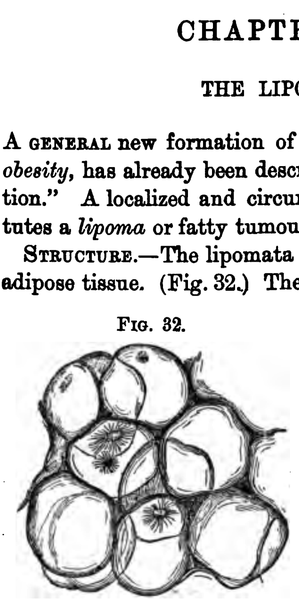
CHAPTER XV.

THE LIPOMATA.

A GENERAL new formation of adipose tissue constituting *obesity*, has already been described under "fatty infiltration." A localized and circumscribed formation, constitutes a *lipoma* or fatty tumour.

STRUCTURE.—The lipomata resemble in their structure adipose tissue. (Fig. 32.) They consist of cells containing fat, and a variable quantity of common connective tissue. The cells, like those of adipose tissue, though usually somewhat larger, are more or less round or polygonal in shape, and are distended with fluid fat. The nucleus and protoplasm are so compressed against the cell-wall by the fluid contents, that although their existence may often be demonstrated by treatment with reagents, they are usually only readily visible when the cell is atrophied and contains less fat. (See Fig. 2 *a*.) The connective tissue, which varies in amount, unites the cells in masses or lobules of various sizes, and also in most cases forms a *capsule* around the tumour. Blood-vessels are distributed in the fibrous septa.

FIG. 32.



Lipoma. Some of the cells contain crystallized fatty acids. × 200.

Development.—The lipomata grow from adipose, or from common connective tissue. Adipose tissue, it must be remembered, is merely connective tissue containing numerous cells which are infiltrated with fat; and its growth consists, either in the infiltration of more of these cells, or in a proliferation of the cells, and an accumulation of fat in those newly developed. A lipoma in the same way originates by a localized proliferation of cells, which as they are produced become infiltrated with fat. The growth of these tumours is always very slow, and they are usually encapsuled by a layer of fibrous tissue.

Secondary Changes.—Secondary changes in the lipomata are not common; their fibrous septa may, however, become calcified, or even ossified, and the fatty tissue undergo a process of liquefaction. Softening may also occur from a mucoid change. Sometimes they become the seat of an inflammatory process; then, when situated in the subcutaneous tissue, the skin over them becomes adherent and ulcerates, and a fungating mass is the result.

Physical Characters, &c.—The situation of the lipomata is almost co-extensive with that of adipose and connective tissue. They occur most frequently, however, in those parts in which fat is normally met with, as in the subcutaneous tissue, the inter-muscular septa, and in the connective tissue of glands. They also occur in the subsynovial tissue, and in the submucous tissue of the stomach and intestines. They sometimes attain an enormous size. They are lobulated, and are usually surrounded by a fibrous capsule which separates them from the adjacent structures. On section they present the ordinary appearance of adipose tissue. Their consistence varies with the amount of fibrous tissue which they contain. They are usually single, though not unfrequently multiple. In their growth they sometimes become pedunculated.

Clinical Characters.—Clinically the lipomata are *perfectly innocent.*

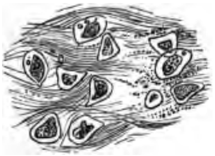
CHAPTER XVI.

THE ENCHONDROMATA.

THE Enchondromata are tumours histologically resembling cartilage.

STRUCTURE.—Like cartilage they consist of cells and an intercellular substance, which present all the variations observed in the normal tissue. (Fig. 33.) The intercellular substance may be hyaline, faintly or distinctly fibrous, or mucoid. When fibrous, the fibres may be arranged like those of fibrous-cartilage, or more or less concentrically around the cells as in the reticular cartilages of the ear and larynx. The cells may be very numerous, or few in proportion to the matrix. They are round, oval, spindle-shaped or stellate. In the hyaline forms they are usually large and round or oval; in the fibrous forms they are often smaller and spindle-shaped, more resembling those of connective tissue; and in the mucoid forms, they are more commonly stellate and branched, like those of the umbilical cord. They are either single or arranged in groups, and are usually surrounded by a fibrous capsule, though this is often very *indistinct*. They enclose one or more nuclei and slightly granular contents; sometimes a cell-wall cannot be dis-

FIG. 33.



Enchondroma. × 200.

tinguished. In addition to the intercellular substance, the growth is usually divided into several lobes, by bands of fibrous tissue; these lobes are often very distinct, so that the growth appears to be made up of several separate tumours. The fibrous tissue in most cases also encapsules the growth and separates it from the surrounding structures. The vessels, which are usually not very numerous, are distributed in the fibrous septa.

DEVELOPMENT.—The enchondromata most frequently originate from bone and common connective tissue, very rarely from cartilage. Cartilage itself, and especially fibrous-cartilage, is very closely allied to common connective tissue. It grows from the deeper layers of the perichondrium, which proliferate and form an embryonic tissue; the young cells become cartilage-cells, and these probably form the matrix, which is either homogeneous or fibrillated, constituting in the one case hyaline, and in the other fibrous cartilage. The development of enchondroma from connective tissue is precisely similar to the physiological process.

In the development of enchondroma from osseous tissue, the medulla is the source of the new growth. This proliferates, the osseous trabeculæ are absorbed, the neighbouring medullary spaces open one into the other, and in this manner a large medullary cavity is produced. In the centre of this, the young cells first formed enlarge and become separated by a homogeneous, or less frequently, slightly fibrillated intercellular substance, and thus is produced a mass of cartilage in the centre of the medullary tissue. This gradually increases till ultimately a layer of fibrous tissue is formed around it, and its further growth takes place from the tissue of its capsule.

Lastly, cartilaginous growths may originate from cartilage itself. These are seen on the surface of the articular *cartilages in chronic* rheumatism, and sometimes on the costal and intervertebral cartilages. They are simply local outgrowths from pre-existing cartilage. They rarely attain a large size, and in structure and physical characters more closely resemble normal cartilage than the other forms of enchondroma. They are often described as *enchondroses*.

Secondary Changes.—Of these, calcification is much the most common. It affects different parts of the growth, commencing in the capsules, and then involving the intercellular substance. Ossification also occasionally occurs; it commences at separate centres, and spiculæ of bone are formed which traverse the tumour in various directions. Fatty degeneration and mucoid softening are common changes, and may lead to the formation of large softened masses which present the appearance of cysts. In rare cases the skin covering the tumour ulcerates, and a fungating mass protrudes.

Varieties.—The varieties of enchondroma depend upon the nature of the intercellular substance. There are thus hyaline, fibrous, and mucoid enchondromata; these, however, are usually combined in various degrees in the same tumour. As a rule, those originating from the medulla of bone are of the hyaline and mucoid class, whilst those originating from connective tissue in other situations are more frequently fibrous. The rapidly growing fibrous forms approach very closely the confines of the sarcomata, the mucoid forms the confines of the myxomata: and these varieties often appear to be associated in the same tumour.

A variety of enchondroma has been described under the name of *osteo-chondroma*, which in structure more closely resembles bone than cartilage. It consists of a tissue similar to that met with between the periosteum and bone in rickets, which from its resemblance to osseous has been called *osteoid* tissue. This tissue only requires *calcifying* to become true bone. Like bone it is made up of trabeculæ and medullary spaces, but the trabeculæ, instead of bone-corpuscles and lamellæ, consist of small angular cells without a capsule, situated in an obscurely fibrillated matrix, which in part is calcified. The medullary spaces contain a fibrous stroma and many blood-vessels. The osteo-chondromata, although consisting mainly of this osteoid tissue, contain also a small proportion of cartilage. They originate beneath the periosteum, their common seat being the ends of the long bones. Their growth is very rapid, and they often attain an enormous size. They are much more freely supplied with blood-vessels than the ordinary enchondromata, and hence they are much less frequently the seats of retrogressive changes. They are especially prone to become ossified, and converted into true bone.

Physical Characters, &c.—The enchondromata occur most frequently in early life. About three-fourths of them are met with in the osseous system, where they grow either from the medulla or from the periosteum: their favourite seat is the extremities of the fingers and toes. The remaining fourth occur most frequently in the parotid gland and in the testicle. They occasionally grow in the subcutaneous cellular tissue of the mammæ, and in the lungs. They are usually single except when occurring on the fingers and toes, in which situations they are more frequently multiple. They consist of a single tumour, or of several smaller tumours held together by fibrous tissue. Their consistence is softer than that of cartilage, sometimes it approaches that of a soft jelly. Their growth is usually slow, though in the softer forms and in those growing in the medulla of bone, it is often very rapid. They may attain an enormous size.

Clinical Characters.—The enchondromata must for the most part be regarded as innocent growths. Those homologous forms which originate from cartilage, and have been called "enchondroses," differ in all respects from the heterologous, and never exhibit malignant characters. The more heterologous forms originating from connective tissue and bone, are usually encapsuled, and in most cases produce merely local effects, although these, from the parts involved and the rapidity of growth, are often very injurious. The softer forms, however, and especially those which occur in the medulla of bone, occasionally exhibit malignant characters. These grow the most rapidly, and are sometimes not limited by a fibrous capsule; they may therefore recur locally after removal. In rare cases they have also infected the lymphatic glands, and recurred in the lungs.

In speaking of the malignancy of the enchondromata, it must be borne in mind how frequently these cartilaginous growths are associated with sarcoma; so that whilst it must be admitted that pure enchondromata are in exceptional cases malignant, the malignant properties ascribed to these growths are often due to their combination with sarcomatous elements.

CHAPTER XVII.

THE OSTEOMATA.

The Osteomata or osseous tumours, are tumours consisting of osseous tissue. A new formation of bone occurs under various circumstances. Irritative conditions of the bone and periosteum are often attended by a large formation of new bone. This is seen after fractures, in which there is not only a formation of bone from the bone itself, but also from the periosteum and adjacent fibrous structures ("permanent" and "provisional callus"). Chronic inflammation of the periosteum is also frequently followed by thickening of the bone beneath it. These, however, are inflammatory formations, and have not an independent growth like the osseous tumours.

Structure.—Osseous tumours resemble in structure normal bone. There are three varieties:—

1. *The Eburnated Osteomata.*—These consist of dense, compact, osseous tissue. The lamellæ are arranged concentrically and parallel to the surface of the tumour. There is a complete absence both of blood-vessels and of cancellous tissue.

2. *The Compact Osteomata.*—These are formed of a tissue similar to that of the compact tissue of the long bones; differing only in the arrangement of the Haversian canals and canaliculi, which is less regular than in normal bone.

3. *The Cancellous Osteomata.*—These consist of cancellous osseous tissue. The medullary spaces may contain embryonic tissue, a fibrillated tissue, or fat.

DEVELOPMENT.—Osseous tumours, like normal bone, can originate only from cartilage or from connective tissue. In both cases the process is precisely similar to that of physiological ossification.

VARIETIES. — The osteomata are divisible into two classes, according to their seat—the homologous osteomata or *exostoses*, and the heterologous osteomata or *osteophytes*.

The *homologous osteomata* or *exostoses*, are outgrowths from pre-existing bone, growing either from the periosteum, from the articular cartilage, or from the medulla. Those growing from the periosteum occur most frequently on the external and internal surfaces of the skull; the orbit is an especially favourite seat, and here they are often dense and eburnated. They are also common on the upper and lower jaws, and in this situation they may grow from the dental periosteum. There is usually a line of demarcation between them and the subjacent bone, the new tissue of the tumour being distinct from the compact tissue of the bone. The periosteum from which they grow covers them, and is continuous with that of the old bone.

The exostoses growing from the articular cartilages occur at the ends of the long bones. In structure they are much more cancellous than the periosteal growths, and their outline is less regular. The medullary exostoses —or more properly, *en-ostoses*—are the least frequent: they originate in the medullary tissue.

The *heterologous osteomata* or *osteophytes*, originate apart from bone, growing from the connective tissue or from cartilage. They are much less common than the *homologous* growths, and must in most cases be regarded rather as inflammatory formations than as tumours.

Such formations of bone are met with in tendons, in the cartilages of the larynx in chronic laryngitis, in the bronchi, in articular synovial membranes, in muscle, in the arachnoid and pia mater, and occasionally in the lungs and brain. They must be distinguished from calcareous deposits, in which there is no new formation. (See "Calcareous Degeneration.")

CLINICAL CHARACTERS. — The osteomata are perfectly innocent tumours. Their growth is very slow, although they sometimes attain a considerable size. They are often hereditary and multiple, in which case they usually occur in early life. Those osseous growths which sometimes exhibit malignant characters, are sarcomata, enchondromata, or cancers which have undergone partial ossification. From these, true osteomata must be carefully distinguished.

CHAPTER XVIII.

THE LYMPHOMATA.

THE Lymphomata are new formations consisting of lymphatic, or, as it is sometimes called, *adenoid* tissue (the "adenoid tissue of His"). Lymphatic tissue is the tissue composing the follicles of the lymphatic glands and the Malpighian corpuscles of the spleen, and existing in many other organs belonging to the lymphatic system. This tissue is now known to have a much more general distribution than was formerly supposed; it not only constitutes the follicles of the lymphatic glands and the Malpighian corpuscles of the spleen, but also Peyer's glands and the solitary glands of the intestine, the follicles of the pharynx and tonsils, the Thymus gland, and the trachoma glands of the conjunctiva. Recently it has also been found to exist in many other situations, as around the blood-vessels of the pia mater and of other parts, in the peri-bronchial connective tissue, in the pleura immediately beneath its endothelium, in the peritoneum, in the mucous membrane of the alimentary canal, and in the medulla of bone.

STRUCTURE.—Lymphatic tissue, wherever it exists, possesses the same general structure, and the follicle of a lymphatic gland may be taken as the type, not only of the physiological tissue, but also of the pathological growths.

This tissue consists essentially of a delicate reticulum, within the meshes of which are contained lymphatic cells —the so-called lymph-corpuscles. The reticulum is made up of very fine fibrils, which form a close net-work, the meshes of which are only sufficiently large to enclose a few, or even a single corpuscle, in each. The fibrils usually present a more or less homogeneous appearance, and, as in the stroma of a lymphatic gland, nuclei are often to be distinguished at the angles of the net-work.

The lymphatic cells, or lymph-corpuscles, which constitute the greater part of the tissue, can in most cases be readily isolated from the meshes of the reticulum. They are identical in their characters with the white corpuscles of the blood, and like these are contractile, and possess the power of spontaneous movement. As usually seen after death, they are spheroidal, pale, semi-transparent bodies, varying considerably in size, and also presenting slight differences in their structure. Some are granular and appear to possess no nucleus; in others, a distinct, simple, or compound nucleus is visible, which is usually also granular; others again are much larger and contain two or even three nuclei. These larger elements containing more than one nucleus, are only met with during the process of rapid growth. (See Fig. 35.)

Development.—The lymphomata originate for the most part from lymphatic tissue, being simply overgrowths of pre-existing lymphatic structures. At the same time it is probable that the new elements are in some cases partly derived from migrated blood-corpuscles, which multiply subsequently to their escape from the vessels. (See "Leukæmia.") These growths are therefore usually homologous. They may, however, be in a certain sense heterologous, either owing to the new tissue extending considerably beyond the confines of the old, or to its growth in situations where it is normally almost entirely *wanting.*

VARIETIES.—The lymphomata include the three following varieties:—*simple lymphoma, lymphadenoma*, and *leukæmia*. Each of these must be considered separately.

SIMPLE LYMPHOMA.

A simple non-inflammatory enlargement of a lymphatic gland, not resulting from any obvious irritation, undergoing no extensive retrogressive changes, and like a tumour having a tendency continually to increase, may be called a *simple lymphoma*.

The enlargement is probably owing to a hyperplasia of the elements of the gland—a hyperplasia which is characterized by its *chronicity*, and *tendency to continue*. Whether the migration of blood-corpuscles takes any part in the process is unknown. The newly-formed elements undergo no marked retrogressive changes, and hence the size of the gland becomes permanently increased. The lymph-corpuscles throughout the gland increase in number, many of them at the same time increase in size, and the larger cells often contain more than one nucleus. If this general hyperplasia is rapid, the gland becomes soft and pulpy in consistence, and the cortical and medullary portions may be no longer distinguishable. As the growth continues, there is usually at the same time an increase in the stroma of the gland, the trabeculæ and capsule become denser and more fibrous, so that ultimately the consistence of the enlarged gland may be firmer than natural. The slower and more chronic the growth, the greater is the increase in the fibrous structures.

Sometimes the enlargement of the glands appears in the first place to be of an inflammatory nature, and to result from some irritation, but upon this being removed, the glands instead of subsiding continue to increase. In *most cases*, however, no such source of irritation is *discoverable*.

The glands which are especially prone to this disease, are the cervical, the submaxillary, the axillary, the inguinal, the bronchial, and the abdominal glands. Usually only a single gland or a single group of glands is affected; sometimes, however, the growth is more general. As the glands enlarge, they gradually unite, so that ultimately they may form very large lobulated tumours.

The lymphatic structures in the intestine may in the same way become enlarged, and project so as to form polypi. The enlargement of the spleen in ague, is also probably of the same nature.

LYMPHADENOMA.

Closely allied to the simple lymphomata are the growths now known as *lymphadenoma*. These growths were formerly described by Hodgkin, Bright, Wilks, and Trousseau; and the condition in which they are met with was called, after the first-named of these observers, "Hodgkin's Disease." Trousseau designated it "Adénie." Recently their characteristics have been more fully determined by MM. Cornil and Ranvier, and by Drs. Murchison* and Sanderson, to whose descriptions the reader is referred for more complete information respecting them.

The disease consists in a hyperplasia of the lymphatic glands and of other lymphatic structures, together with the development of lymphatic growths in various organs. Histologically, the new growths are precisely similar to those of leukæmia. The disease differs essentially, however, from leukæmia in this respect, that the new formation of lymphatic tissue is not associated with any notable increase in the number of the white corpuscles in the blood.

The lymphatic glands are usually the earliest seats of the new growth, and here it differs in no respect anatomically from what has been described as "simple lymphoma." At first it may be limited to a single group of glands; subsequently, however, the process often becomes more general, and the glands throughout the whole body may be more or less involved. The glands as they increase in size gradually become confluent so as to form large lobulated tumours, and the new growth, which takes place in the earlier stages within their capsules, in most cases ultimately extends so as to infiltrate the surrounding structures. When commencing in the bronchial glands, for example, the growth may gradually involve one or both lungs, and it constitutes in this situation the most common variety of mediastinal tumour.

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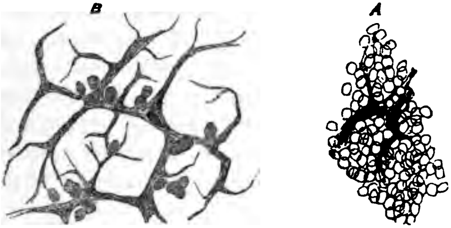
* "*Trans. Path. Soc. Lond.*" vols. xx. and xxi.

This new growth of lymphatic tissue, which commences in and usually extends beyond the confines of the lymphatic glands, is often ultimately followed by the formation of lymphatic growths in various internal organs. In the spleen, the Malpighian corpuscles become enlarged and form greyish-white nodules and masses. The liver, kidneys, lungs, stomach, muscle, bones, and subcutaneous tissue may all become involved, the new growths occurring either as nodules of various sizes scattered through the organs, or in a more infiltrated form, like many of the growths met with in leukæmia.

With regard to the structure of the new growths—they resemble in the main lymphatic tissue (the "adenoid tissue of His," Fig. 34); they present, however, certain histological differences in the various stages of their development, differences which correspond with those met with in inflammatory conditions of a lymphatic gland. In the earlier stages of their growth, when this is rapid, the small lymph-corpuscles are often associated with much larger cellular elements which contain one, and in some cases several nuclei. (Fig. 35.) These larger cells are frequently met with in lymphatic structures which are undergoing active growth. They somewhat resemble the multi-nucleated masses of protoplasm ("myeloid cells") which occur in certain connective tissue-growths.

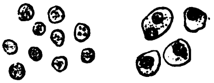
FIG. 34.



Lymphadenoma.—A, a thin section of a lymphadenomatous tumour of the mediastinum. B, a similar section, from which most of the cells have been removed by pencilling, so as to show the reticulated network. This network is much more marked than that often met with. × 200.

(See "Genesis of Cells.") In a more advanced stage these larger cell-forms are often almost entirely wanting; the reticulated stroma, which at first is extremely delicate, usually becomes more marked, denser, and more fibrous; and with this increase in the fibrous reticulum, the lymph-corpuscles gradually diminish in number and become arranged in smaller groups within its meshes. Sometimes nuclei are to be seen in the angles of the reticulum similar to those in the stroma of a lymphatic gland. The gradual increase and thickening of the

FIG. 35.



Cells from a Lymphatic Growth in the Liver: Those to the left are the ordinary lymph-corpuscles which constituted the greater part of the growth. To the right are some of the larger multi-nucleated elements. × 350.

reticulum is very analogous to what occurs in chronic inflammatory processes in lymphatic glands. (See "Chronic Inflammation of Lymphatic Structures.")

In their physical characters the new growths vary. They are usually of a greyish-white colour and of a soft brain-like consistence, yielding a milky juice which is rich in cellular elements precisely resembling leucocytes. In other cases they are much firmer in consistence, and they may be as hard as an indurated lymphatic gland. These differences depend upon the relative proportion of the stroma. They have but little tendency to undergo retrogressive changes.

Clinically, these growths are exceedingly malignant. They infiltrate the surrounding structures, and often reproduce themselves in internal organs.

LEUKÆMIA.

Leukæmia is a disease characterized by a permanent and continuous increase in the number of the white corpuscles in the blood, which increase is associated with a new formation of lymphatic tissue in the spleen, in the lymphatic glands, and sometimes in other organs. Respecting the relation which subsists between the new growth of lymphatic tissue and the increase in the number of the white blood-corpuscles—it is probable, as stated by Virchow, that the former is a cause of the latter, and that the increase is partly due to a larger number of lymphatic elements entering the blood than in health. At the same time it is difficult to admit this as the only cause of the increase, as new growths of lymphatic tissue may take place in these organs without the production of any leukæmia. This has been seen to occur in lymphadenoma. It is possible that the power of the white blood-corpuscles and lymph-corpuscles to form red *corpuscles* is diminished, or that the white corpuscles *may increase* by multiplication in the blood.

The new formation of lymphatic tissue is in the first place *hyperplastic*, taking place in the spleen or in the lymphatic glands; subsequently, however, it may become *heteroplastic*, and the liver, the kidneys, the lungs, and other organs, may become infiltrated with lymphatic elements. The growth is a *continuous* one; the new elements many of them enter the blood, the remainder, not undergoing any retrogressive changes, give rise to tumours in, or to a general increase in the size of, the organs in which they are generated.

The new growth may commence in the spleen or in the lymphatic glands. In most cases the spleen alone is involved. Sometimes the growth in the spleen is associated with a similar one in the lymphatic glands. In rare cases, the lymphatic glands are the sole seats of the hyperplastic process.

In the *spleen*—which must thus be regarded as the most important organ in the production of leukæmia—the first stage in the process is one of intense hyperæmia. The organ becomes exceedingly vascular, and the cells both of the pulp and of the Malpighian corpuscles increase in number. The process, however, soon becomes principally limited to the Malpighian corpuscles. In these, the cells continue to multiply rapidly, many new blood-vessels are formed, and the corpuscles thus increase in size. They sometimes attain the size of a hazel-nut, and are seen as firm whitish nodules of an irregular shape, scattered through the much enlarged and vascular organ. As the Malpighian corpuscles increase in size, the surrounding pulp gradually atrophies, and often becomes deeply pigmented. The trabeculæ at the same time becomes thicker and more fibrous. The organ thus becomes firmer in consistence, and the enlarged Malpighian corpuscles make up the chief part of its bulk. The capsule also becomes thickened, and forms adhesions with the surrounding viscera.

In the *lymphatic glands* the process is precisely similar to that in the spleen, the follicles of the gland being the chief seats of the hyperplasia. The glands become enlarged, soft, and vascular.

In course of time the disease may become *heteroplastic*, and a large formation of lymphatic tissue take place in organs in which normally it is almost entirely wanting. This heteroplastic tissue probably consists for the most part of white blood-corpuscles, which have migrated from the enlarged and dilated vessels, and have infiltrated the surrounding structure; it must, therefore, be regarded as more distinctly an *infiltration* than are many of the new formations.

The organ which is the most frequent seat of the heteroplastic growth, is the *liver*. Here the vessels throughout the organ become enlarged and distended with white blood, and the infiltration commencing in the interlobular tissue, gradually extends into the lobules themselves. The lobules thus become gradually enlarged. In the earlier stages, they are seen to be clearly mapped out by the greyish-white interlobular infiltration. As the infiltration increases the liver-cells become compressed and atrophy, until ultimately the lobules may be replaced entirely by lymphatic tissue, and stand out as greyish-white masses upon the cut surface of the organ. Associated with this infiltration there is often a formation of small, round, soft, whitish nodules, somewhat resembling grey tubercles. Owing to these changes, the liver becomes very considerably increased in size.

In the *kidney*, which is also frequently affected, the change is similar to that in the liver. Here also it consists for the most part in an infiltration, with which may be associated the formation of roundish nodules and masses. Other organs are much less frequently involved—*the lungs*, pleuræ, stomach, intestines, and heart, may all, *however*, become the seats of the heteroplastic formations.

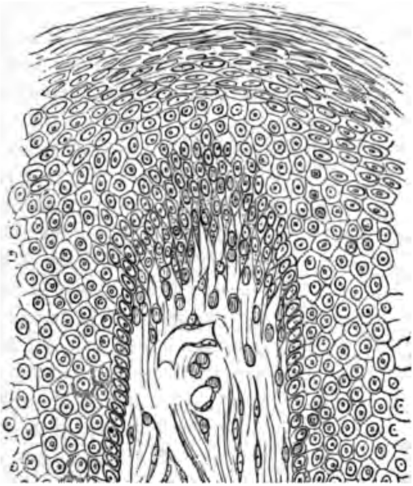
CHAPTER XIX.

THE PAPILLOMATA.

THE Papillomata are new formations resembling in structure ordinary papillæ, and like these they grow from cutaneous, mucous, or serous surfaces.

STRUCTURE.—They consist of a basis of connective tissue, supporting blood-vessels, which terminate in a capillary net-work or in a single capillary loop, the whole *being enveloped in a* covering of epithelium. (Fig. 36.)

FIG. 36.



Papilloma. Showing a single enlarged papilla. (Rindfleisch.)

The epithelial covering varies in character in different growths. In those of the skin, it is like that met with in this situation, hard and stratified, and is usually very abundant, forming a dense firm covering. In those originating from mucous surfaces, the epithelium forms a thinner investment, and is of a much softer consistence; whilst in those growing from serous membranes it often constitutes only a single layer.

The growth may be simple—consisting merely of enlarged papillæ, as in a common wart; or it may be more complex, the papillæ being very numerous, and giving off secondary and tertiary offsets. If the investing epithelium is very abundant, it may so enclose the whole mass as to give to it a more or less regular outline. More commonly, however, this is not the case, and the epithelium not being sufficient to fill up the spaces between the papillæ, the growth presents a branched, villous, or cauliflower appearance. The blood-vessels are often very numerous, and are sometimes dilated and tortuous.

Development.—The papillomata always originate from the skin, from mucous, or from serous membranes. They most frequently grow from pre-existing papillæ; sometimes, however, they occur where no papillæ exist, springing directly from the sub-epithelial connective tissue:—this is the case in the stomach and larynx. Their growth is usually slow. The individual tumours rarely attain a very large size, the larger forms being for the most part constituted of several smaller growths.

Secondary Changes.—Of these, ulceration and hæmorrhage are the most frequent. They occur especially in those growths which originate from mucous surfaces. The hæmorrhage is often very abundant, and may even endanger life. This is not unfrequently the case in the papillary growths of the bladder and intestine.

Varieties.—The varieties of papillary tumours depend principally upon their seat. Those growing from the skin are *warts* and *horny growths*. These are firm, have a dense epithelial covering, and are less prone to ulceration and hæmorrhage than those growing upon other parts. Larger and more vascular forms may, however, occur on cutaneous surfaces—such are the *condylomata* and *venereal warts* met with around the anus and upon the external male and female genital organs.

The papillomata of mucous membranes are softer and more vascular than the preceding, they have a less dense epithelial covering, and are more prone to ulceration and hæmorrhage. Many of them come within the category of mucous polypi. They are met with on the tongue, in the larynx and nose, on the gastro-intestinal mucous membrane, on the cervix uteri, and in the bladder. In the bladder and intestine they are often exceedingly vascular, and give rise to profuse hæmorrhage. Here they are not unfrequently confounded with villous epithelioma.

Papillomata of serous membranes never form distinct tumours. They are met with most frequently as small out-growths from the synovial membrane in chronic diseases of joints.

Clinical Characters.—Clinically, the papillomata are innocent growths. They may, however, prove fatal from continuous ulceration and hæmorrhage: this is especially the case, as already mentioned, in papilloma of the bladder and intestine. In these situations they are easily mistaken for epithelioma; the symptoms of both are very similar, and it is often only after death that they can be distinguished. In the papillomata the epithelium is *homologous*, being situated only *upon the surface* of the papillæ, and in no case growing *within* their connective tissue basis. In the epitheliomata, on the other hand, it is *heterologous*, and is met with at the base of the tumour in the subjacent connective tissue. (See "Epithelioma." Fig. 45.)

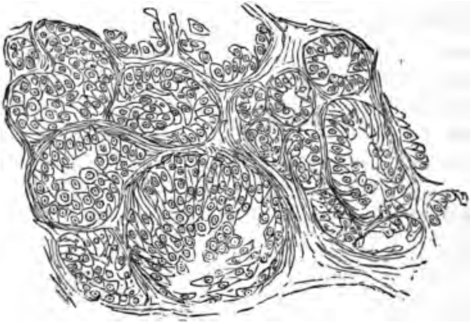
CHAPTER XX.

THE ADENOMATA.

THE Adenomata—or as they are more commonly called, *glandular tumours*—are new formations of gland-tissue.

STRUCTURE.—In structure the adenomata resemble the racemose or tubular glands. They consist of numerous small saccules or tubes filled with squamous or cylindrical epithelial cells. These are grouped together, being merely separated by a small, though varying, amount of connective tissue, in which are contained the blood-vessels. (Fig. 37.)

FIG. 37.



Adenoma of the Mamma. × 300. (Rindfleisch.)

DEVELOPMENT.—The adenomata always originate from *pre-existing* gland-structures, of which they are simply *local hyperplasias.* Their growth, which is usually slow, takes place by the development of diverticula from the saccules or tubules of the gland, and by a proliferation of the enclosed epithelium. The new growth may remain in intimate relation with the adjacent gland, or it may ultimately become separated from it by a fibrous capsule.

Secondary Changes.—The most frequent of these is fatty degeneration of the epithelium, which may give rise to the formation of small caseous masses in the growth. Dilatation of the saccules and tubules so as to form cysts, and mucoid softening, are also common.

Varieties. — One of the seats of adenoma is the mammary gland. Here two varieties must be distinguished,—one, in which there is a general hyperplasia of the whole gland; the other, in which the process is limited to a single, or to a small group of lobules. The former constitutes hypertrophy of the mamma, the latter is the *chronic mammary* or *adenoid* tumour. Adenoma of the mamma is comparatively rare. Many growths in this situation, described as adenomata, are sarcomatous tumours, in which are contained the acini of the gland. The distinction between true adenoma and such sarcomatous growths is often exceedingly difficult. The adenomata are either superficial or deeply seated in the gland from which they originate, and from which they are usually separated by a loose fibrous capsule. They are commonly round or oval in shape, lobular, and of a hard elastic consistence. On section they present a lobulated appearance, their racemose structure being often visible to the naked eye.

The glandular structures of mucous membrane are also very common seats of adenoid growths. In the nose, the pharynx, the stomach, the intestines, the vagina and uterus, these growths are frequently met with. In course of time they usually gradually project above the surface of the membrane so as to form a polypus, and thus constitute one of the most common forms of mucous polypi.

In consistence they are soft and somewhat gelatinous, and often present a semi-translucent appearance. Their surface resembles in colour the surrounding mucous membrane. The formation in them of cysts, by the dilatation of their tubules, is exceedingly frequent: the cysts usually contain a soft mucoid substance.

The other seats of adenomata are the sebaceous glands, the pineal gland, and the ovaries.

CLINICAL CHARACTERS.—Clinically, the adenomata are for the most part perfectly innocent; they are, however, very liable to be confounded with growths possessing malignant properties. A tumour, also, which is primarily a simple adenoma, may subsequently become cancerous. The anatomical distinction between cancer of a gland, in its earlier stages, and a simple glandular tumour, is often exceedingly difficult, especially in the mamma. In cancer the growth commences by a proliferation of the epithelium within the ducts of the gland; and as the epithelium only subsequently becomes heteroplastic, the determination of the nature of the tumour in this stage is necessarily attended with considerable difficulty. In sarcomatous tumours, again, originating in the connective tissue of a gland, the ducts of the gland filled with epithelium, are often seen embedded in the new growth, and thus the appearance of adenoma may be closely simulated.

CHAPTER XXI.

THE CARCINOMATA.

THE Carcinomata, or Cancers, are new formations consisting of cells of an epithelial type, without any intercellular substance, grouped together irregularly within the alveoli of a more or less dense fibroid stroma.

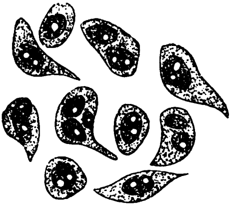
The term "*cancer*" has been so commonly applied indefinitely to any growth possessing malignant properties, that "*cancerous*" and "*malignant*" have come to be regarded by many as synonymous terms. It is important, however, clearly to distinguish between them. A *cancer* is a growth possessing the above-named definite structure; a *malignant* growth, on the other hand, is one which, independently of its structure, tends to reproduce itself in adjacent or distant tissues. (See "Malignancy.") "Cancerous," is an *anatomical* term; "Malignant," is a *clinical* one.

The Cancers include the four following varieties:—*Scirrhus*, *Encephaloid*, *Colloid*, and *Epithelioma*. These, although all possessing the same general characters, present certain structural and clinical differences which serve to distinguish them. It will be well in the first place to describe the characters common to the whole class, and subsequently those which are peculiar to the individual members.

STRUCTURE.—*In* structure, the Cancers so far resemble one another, that they all consist of cells of an epithelial type, without any intercellular substance, grouped together irregularly within the alveoli of a fibroid stroma. Although there is no distinct intercellular substance, a certain amount of fluid exists between the cells. It is this fluid which exudes from the freshly-cut surface of the cancer, and the number of cells which it contains give to it a milky appearance.

The *cells* are characterized by their large size, by the diversity of their forms, and by the magnitude and prominence of their nuclei and nucleoli. (Fig. 38.) In size they vary from $\frac{1}{600}$ to $\frac{1}{1500}$ of an inch in diameter; the majority being about five times as large as a red blood-corpuscle. They are round, oval, fusiform, caudate, polygonal—exhibiting, in short, every diversity of outline. These variations in form are principally owing to the mutual pressure to which in their growth they are subjected. The nuclei, which are large and prominent, are round or oval in shape, and contain one or more bright nucleoli. The nuclei are, perhaps, most frequently single; two, however, are frequently met with, and in the softer and more rapidly growing cancers they may be much more numerous. The cells rapidly undergo retrogressive changes, hence they usually contain molecular fat. They are many of them exceedingly destructible, so that often

FIG. 38

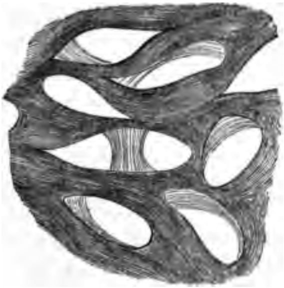


Cells from a Scirrhus of the Mamma. × 250.

more free nuclei than cells are visible. Cells precisely similar to these are met with in other morbid growths, and also in the normal tissues. There is thus no *specific* "cancer-cell." It is the general character of the cells, together with their mode of distribution in the meshes of a fibroid stroma, that determines the nature of the growth to which they belong.

The *stroma* varies considerably in amount, being much more abundant in some varieties of cancer than in others. It consists of a more or less distinctly fibrillated tissue, arranged so as to form alveoli of various forms and sizes, within which the cells are grouped. (Fig. 39.) These alveoli communicate with one another so as to form a continuous cavernous system. The characters of the stroma vary with the rapidity of its growth:—if this is rapid, it will contain some round and spindle-shaped cells; if, on the other hand, it is slow or has altogether ceased, the tissue will contain but few cells, and will be denser and more fibrous in character. The latter is the condition in which it is most commonly met with.

FIG. 39.



The Alveolar Stroma from a Scirrhus of the Mamma. The cells have been removed by pencilling. × 200.

Within the stroma are contained the blood-vessels.

These are often very numerous, and form a close network. They are always limited to the stroma, and in no case do they encroach upon the alveoli. This distribution of the blood-vessels is important as distinguishing the cancers from the sarcomata. In the latter the vessels are not supported by a stroma, but ramify amongst the cells of the growth; hence the facility with which these tumours become generally disseminated.

In addition to the blood-vessels the cancers also possess *lymphatics*. These accompany the blood-vessels, and, as has been shown by MM. Cornil and Ranvier, communicate with the alveoli; hence the great tendency of cancer to infect the lymphatic glands.

DEVELOPMENT.—The question of the genesis of cancer involves that of the genesis of epithelium generally. It is maintained by many Histologists that epithelium can only originate from epithelium, and that the strata of cells set aside in the embryo for the production of the epithelial tissues, is the source from which all epithelium is subsequently derived. Others admit that epithelium may also originate from connective tissue. (See "Development of the New Formations.") A like difference of opinion exists as to the source of the epithelial-like cells of cancer. By many—as Waldeyer, Thiersch, and Billroth—they are regarded as originating only from pre-existing epithelium. Others — amongst whom are Virchow, Lücke, Rindfleisch, and Klebs—maintain that they may also be derived from cells belonging to the connective tissue.

The difficulty of determining the genesis of cancer, is partly owing to the fact that it so frequently originates in structures where epithelium is normally abundant, as in the mamma, skin, and alimentary canal; and that this normal epithelium is always, from the earliest stage of the growth, the seat of active proliferation. In cancer of the mamma, for example, the first change often observable is a large accumulation of epithelium within the ducts of the gland, a condition similar to that already described as occurring in the development of an ordinary glandular tumour. (See "Adenoma.") Soon, however, the epithelium is found outside the ducts, amongst the inter- and peri-glandular connective tissue, which is also in a state of active proliferation, and is infiltrated with small round cells. The outline of the ducts ultimately becomes completely annihilated, and the epithelial cells are seen in alveoli, formed of a fibroid tissue. The question arises as to whether the epithelial-like cells, which constitute the ultimate cancerous growth, originated from those normally existing within the ducts of the gland, which in the process of development have extended beyond the ducts into the surrounding tissue; or whether they originated in the connective tissue—the proliferation of the glandular epithelium being merely a secondary process, and resulting from the irritation of the inter-glandular growth.

In those rare cases in which cancer occurs primarily in situations where no epithelium normally exists, as in the medulla of bone, and in lymphatic glands, it is difficult to maintain an epithelial origin. It must be admitted, however, that the tendency which is exhibited by the cells of cancerous growths to maintain the type of the epithelial structures in the vicinity of which they grow, is greatly in favour of the view that they are derived from the epithelium. In cancers situated near the cutaneous surfaces, for example, the cells are usually of the squamous type, whereas in those growing in connexion with the glands of mucous membranes, they more commonly resemble the epithelium of the gland. It must be borne in mind, also, that the characters of young epithelium are by no means well defined. It is impossible to draw a line of demarcation between young epithelial cells, and the small round cells which are so numerous in the growing stroma of the *cancer. It would appear* to be quite in accordance with our present state of knowledge to admit the probability of two different modes of origin of the epithelial-like cells in cancer—one from epithelium, and the other from connective tissue: in the former case the cells being more strictly epithelial, such as are met with in epithelioma; in the latter, the epithelial characters being less marked, as in many forms of encephaloid and scirrhus.

The *stroma* is partly a new growth, and partly the pre-existing connective tissue of the part in which the cancer originates. It is probably in the main a new formation, and the pathology of its development will vary with that of the origin of the epithelial elements of the cancer. If the latter originate from epithelium, the stroma may be regarded as the result of the irritation of the connective tissue by the infiltrating epithelial cells. If, on the other hand, the epithelial elements originate from connective tissue, the stroma must be regarded as a portion of the product of the connective tissue hyperplasia.

The cancers in their growth very rarely become encapsuled, but gradually infiltrate the surrounding structures. This process of infiltration is very characteristic, and is more marked in cancer than in any of the malignant growths. The epithelial-like elements are seen infiltrating the tissues for some distance around the confines of the tumour, so that there is no line of demarcation between it and the normal structures.

SECONDARY CHANGES.—The most important of these is fatty degeneration. This always occurs to a greater or less extent in all the varieties of cancer. The more rapid the growth, the earlier does this retrogressive change take place, and the greater is its extent; hence it is usually most marked in encephaloid. It produces softening of the growth, which is often reduced to a pulpy cream-like consistence. Caseation, pigmentation, mucoid and colloid degeneration may also occur. Calcification is very rarely met with.

VARIETIES.—The term "cancer" was so vaguely applied by the older pathologists—nearly all malignant formations being included under this head—that considerable confusion has resulted in the classification of cancerous growths. Peculiarities in situation, structure, and appearance, have given rise to special names, hence the terms—"*osteoid*," "*chondroid*," "*cystic*," "*villous*," and "*hæmatoid*" cancer. A cancer containing large quantities of pigment was described as a distinct variety, under the name of *melanotic* cancer. Melanotic cancer, however, is exceedingly rare. The majority of tumours which are thus designated are in reality sarcomata. (See "Melanotic Sarcoma.")

The most convenient classification, and that which is now generally adopted, divides the cancers into four groups:—*scirrhous*, *fibrous*, or *chronic* cancer; *encephaloid*, *medullary*, or *acute* cancer; *colloid* or *gelatiniform* cancer; and *epithelioma*, or *cancroid*. This division is based principally upon the relative proportion of the stroma, and upon the type of the epithelial elements.

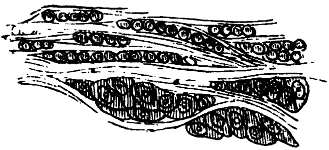
SCIRRHOUS CANCER.

Scirrhous, *fibrous*, or *chronic* cancer is characterized by the large amount of its stroma and by the chronicity of its growth. The slowness in the development of scirrhus probably accounts in great measure for the peculiarities in its structure and physical characters.

The epithelial growth, although at first it may be luxuriant, quickly subsides. The elements soon atrophy and undergo retrogressive changes. They are most abundant in the external portions of the tumour, where growth is taking place; in the central portions they may be almost entirely wanting. (Fig. 40.)

This degeneration of the epithelial-like elements is probably owing to the excessive growth of the stroma, and to the subsequent induration and contraction which it undergoes. It quickly assumes the characters of cicatricial tissue, and becomes hard and indurated. This

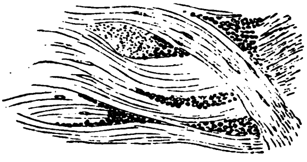
FIG. 40.



Scirrhus of the Mamma. A thin section from the most external portion of the tumour. Showing the clusters of small "indifferent" cells; and more internally, the development of the epithelial-like elements within the alveoli of the stroma. × 300. (Rindfleisch.)

causes obstruction and obliteration of the blood-vessels which it contains, and it is probably to this interference with the vascular supply that the arrest in the development of the cancer is owing. The whole of the central portions of the growth may thus ultimately consist simply of dense fibrous tissue, the circumference being the only part where the epithelial structure is visible.

FIG. 41.



Scirrhus of the Mamma. A thin section from the more central portion of the tumour. Showing the cicatricial tissue which constitutes the older portions of the growth. × 300. (Rindfleisch.)

(Fig. 41.) The amount of atrophy and contraction varies considerably in different cases.

The physical characters of scirrhus are in the same way due to the abundance of its stroma. The growth is firm and hard, and it is often depressed in the centre, owing to the contraction of the cicatricial tissue; this is very characteristic of scirrhus of the breast, where it causes puckering of the superjacent structures. On section the tumour presents a white glistening surface, intersected with fibrous bands. The more external are less firm than the central portions of the growth, and yield on scraping a juice which is rich in nucleated cells, free nuclei, and granules.

Scirrhus is most commonly met with in the female breast, and in the alimentary canal—especially in the pylorus, œsophagus, and rectum. It also occurs in the skin.

ENCEPHALOID CANCER.

Encephaloid, *medullary*, or *acute* cancer, is very closely allied to the preceding, from which it differs merely in the greater rapidity of its growth, the small amount of its stroma, and the consequent softness of its consistence. Encephaloid and scirrhus cannot be regarded as in any way constituting distinct varieties of cancer. There are all intermediate stages between them, and the differences in the rapidity of their growth, and consequently in their structure and physical characters, constitute their only distinctive features.

The epithelial growth in encephaloid is rapid and abundant, and the cells quickly undergo fatty degeneration, so that often more free nuclei than cells are visible. The proportion of stroma is very small, and owing to the rapidity of its growth, it is much less fibrous than that of scirrhus, and does not undergo a similar cicatricial contraction. The blood-vessels are very abundant, and the tissue supporting them being soft and non-resists

hæmorrhage readily takes place.

Encephaloid cancer is of a soft brain-like consis the central portions, where fatty degeneration is most advanced, often being completely diffluent. The tumour is often more or less lobulated. On section, it presents a white pulpy mass, much resembling brain-substance, which is often irregularly stained with extravasated blood.

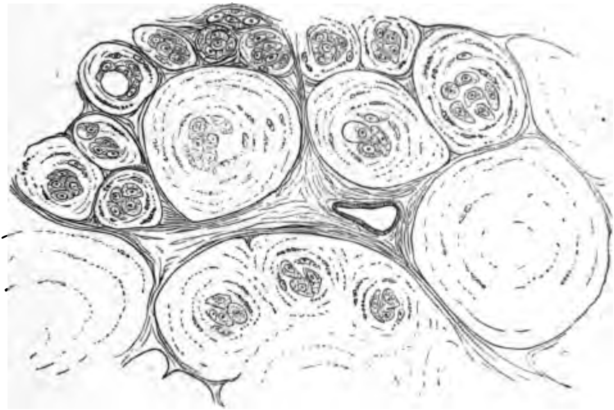
Encephaloid is most frequently met with in internal organs, as a *secondary* growth. It also sometimes occurs primarily, in the articular ends of bones, in the eye, in the testis, and in other parts. Many growths formerly described as encephaloid cancer, are soft sarcomata. (See "Round-celled Sarcoma.")

COLLOID CANCER.

The growths described under the name of *colloid, alveolar,* or *gelatiniform* cancer, although sometimes regarded as constituting a distinct variety of cancer, are simply one of the preceding forms which have undergone a mucoid or colloid change. The frequency with which non-cancerous growths which have undergone these forms of degeneration have been confounded with colloid cancer has already been alluded to. (See "Colloid Degeneration.")

The alveolar structure in colloid cancers is very marked:—the alveoli are large, distinct, and more or less spherical in shape. This large size and distinctness of the alveoli is owing to their distension with the softened substance. Within them is contained the gelatinous colloid material, which is a glistening, translucent, colourless, or yellowish substance, of the consistence of thin mucilage or size-gelatin. In the main it is perfectly structureless; within it, however, are embedded a varying number of epithelial-like cells, which also contain *the same* gelatinous substance. (Fig. 42.) These cells *present* a peculiar appearance:—they are large and spherical in shape, and are distended with drops of the same gelatinous material as that in which they are embedded. (See Fig. 8.) Many of them display a lamellar surface, their boundary being marked by concentric lines. It would appear that the colloid change commences in the cells, which become gradually destroyed in the process. In other cases the cells, with the exception of slight fatty metamorphosis, are unaffected, and the substance distending the alveoli is more viscid and mucoid in character. This is due to a mucoid degeneration of the intercellular substance, rather than to a colloid change commencing in the cells. (See "Mucoid Degeneration.")

FIG. 42.



Colloid Cancer. Showing the large alveoli, within which is contained the gelatinous colloid material. × 300. (Rindfleisch.)

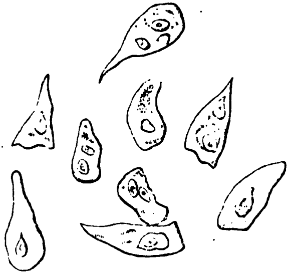
Colloid cancer is most frequently met with in the stomach, in the intestine, and in the peritoneum.

EPITHELIOMA.

Epithelioma, *cancroïd*, or *epithelial cancer*, must be regarded as constituting a much more distinct variety of cancer than either of the preceding. It differs from these in always growing in connexion with a cutaneous or mucous surface, and in its epithelial elements closely resembling the squamous variety of epithelium.

The cells of epithelioma are in the main indistinguishable from those met with on the cutaneous surfaces, and on the mucous membrane of the mouth. They vary in size from $\frac{1}{500}$ to $\frac{1}{1000}$ of an inch in diameter, the average being $\frac{1}{700}$. They contain usually a single nucleus; frequently, however, the nuclei are multiple. (Fig. 43.)

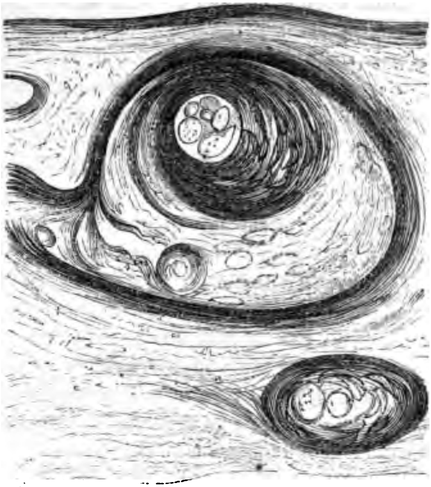
Fig. 43.



Cells from an Epithelioma of the Lip. × 250.

They are often considerably flattened and distorted in shape owing to the pressure to which in their growth they are subjected, but they never present those numerous varieties in outline which are met with in the other varieties of cancer, neither do they exhibit the same marked tendency to undergo fatty degeneration. The *arrangement* of these cells is peculiar:—some of them are *situated* in irregular tubular-shaped lobules; others are less regularly grouped in masses of various sizes amongst the meshes of a stroma. As the cells increase in number they tend to become arranged concentrically in groups, so as to form globular masses. These masses are the "*concentric globes,*" or "*epithelial nests,*" which are so commonly met with wherever squamous epithelium is undergoing rapid growth, and are so especially characteristic of epithelioma. As the epithelium multiplies, the peripheral layers of cells become flattened by pressure against the surrounding structures, whilst those in the centre remain more or less spherical in shape like those of the deeper layers of the epidermis. (Fig. 44.) The *cells may be so closely* packed as ultimately to become

FIG. 44.



Epithelioma of the Lip. Showing the concentric globes of epithelial cells. × 100.

hard and dry like those of the nails and hair, and the globes are then of a brownish-yellow colour and of a firm consistence. These globes are often large enough to be readily visible to the naked eye, and owing to the arrangement of the epidermic scales, they usually present a fibrous appearance.

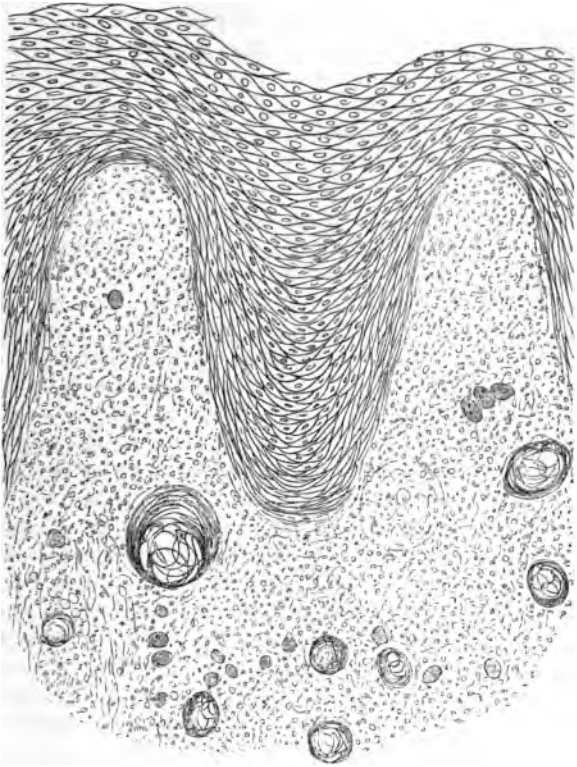
The stroma presents every variation between rapidly growing embryonic, and a completely fibrillated tissue. It may be tolerably abundant, or almost entirely wanting. It rarely forms such a marked alveolar structure as that which characterizes the other varieties of cancer, but usually consists simply of a small-celled infiltration surrounding the epithelial elements, which may ultimately become developed into a more or less completely fibrillated tissue. (Fig. 45.)

With regard to the development of epithelioma—there can be no doubt that its epithelial elements are derived from the epithelium of the skin or mucous membranes, or from that of the glands which are situated in these tissues. The growth commences by a proliferation of this epithelium, which as it increases becomes *heterologous*, extending beyond the normal limits into the subjacent connective tissue, and even into muscle, bone, and other structures (Fig. 45), and it is this heterologous development of epithelium which is the essential characteristic of epithelioma. This extension of the epithelium into the subjacent connective tissue produces in the latter an irritative growth, and thus the groups of epithelial elements are always surrounded by a small-celled ("indifferent") tissue, the small-celled growth preceding the epithelial invasion. (Fig. 45.)

Epithelioma usually presents itself in the first place either as a small foul ulcer with indurated edges, or as a subcutaneous induration or nodule which subsequently *ulcerates*. The surface of the ulcer is frequently papillated *and villous*, owing to the irregular growth of the corium.

The tumour itself is firm in consistence, often more or less friable, and on section presents a greyish-white granular

FIG. 45.



Epithelioma of the Tongue. A thin vertical section, showing the excessive epithelial growth upon the surface of the papillæ, and the extension of the epithelial elements into the subjacent connective tissue. The sub-epithelial tissue is infiltrated with small ("indifferent") cells, amongst which *are seen the epithelial* elements both single and in *groups. × 100.*

surface, sometimes intersected with lines of fibrous tissue. The cut-surface yields on pressure a small quantity of turbid fluid, and in many cases also a peculiar, thick, crumbling, curdy material can be expressed, which often comes out in a worm-like shape, like the sebaceous matter from the glands of the skin. This latter is very characteristic. It is composed of epithelial scales, and on being mixed with water it does not diffuse itself like the juice of other cancers, but separates into minute visible particles. If it is very abundant, the cancer is soft and friable, and the material can be seen in the cut-surface as small scattered opaque dots.

Epithelioma has its primary seat in the immediate vicinity of the cutaneous or mucous surfaces; and it appears in many cases to owe its origin to some external source of irritation. It is most frequently met with in the lower lip at the junction of the skin and mucous membrane, on the tongue, prepuce, scrotum ("chimney-sweep's cancer"), labia, eyelids, cheeks, and in the uterus and bladder. As it extends it may involve any tissue—lymphatic glands, muscle, bone, and tendon may be alike implicated. It very rarely occurs in internal organs.

Epithelial cancers growing from mucous membranes which possess a columnar epithelium, as from the stomach and intestines, differ somewhat from the preceding. They usually originate in the glandular structures of the membrane, and their epithelial elements resemble those of the gland, and are not squamous in character. There is rarely a formation of concentric globes, and the growths are of a soft, and often gelatinous consistence. The distinction between these and simple adenomata is often exceedingly difficult.

Clinical Characters of the Cancers.—In speaking of the clinical characters of the cancers, it is important in the first place to make a distinction between epithelioma and the other varieties. Epithelioma, as far as its malignancy is concerned, occupies a very inferior position to scirrhus and encephaloid. These two latter varieties of cancer possess in the highest degree malignant properties. They extend locally, invading indiscriminately the tissues amongst which they grow, and reproduce themselves in the lymphatic glands and in internal organs. In the process of dissemination, however, they present some peculiarities which distinguish them from growths which are sometimes equally malignant—viz., the sarcomata. The cancers are characterized by their great tendency to reproduce themselves in the neighbouring lymphatic glands. This implication of the lymphatics is much more marked than in the sarcomata, in which it but comparatively rarely occurs, and this is probably owing to the communication of the lymphatic vessels with the alveolar spaces of the cancerous growth. The general dissemination in internal organs, on the other hand, is often effected much less readily in cancer than in sarcoma, and the course of the former is therefore sometimes more protracted than that of the latter. This difference is explained by the difference in the distribution of their blood-vessels:—in cancer, these are contained in the stroma and do not come into contact with the cells of the growth; whereas, in the sarcomata, they ramify amongst the cells, and their walls being composed of thin embryonic tissue like that of the growth which they supply, dissemination through the medium of the blood is rapidly and readily effected. In cancer, the lymph being so important a medium of infection, the reproduction of the growths in internal organs may be considerably delayed; the progress of the disease becomes arrested by the lymphatic glands, and its further dissemination is often only effected after these have become very generally and extensively involved.

With regard to the difference in the clinical characters of the several varieties of cancer—epithelioma, as already stated, is much the least malignant. It extends locally, and may affect the neighbouring lymphatics, but it comparatively rarely reproduces itself in internal organs. This is probably owing to the size and character of its epithelial elements, which render them much less liable to be transmitted by the blood and lymph-streams than are the cells of the other varieties of cancer.

Scirrhus and encephaloid, which anatomically are so closely allied, differ somewhat in the degree of their malignancy. The dissemination of the latter takes place more readily than that of the former, owing to the greater rapidity of its growth, its greater vascularity, and the greater activity of its epithelial elements. Both scirrhus and encephaloid reproduce themselves in the lymphatic glands, and in internal organs. Colloid closely resembles encephaloid, both in the rapidity of its development, and in the degree of its malignancy.

In all the varieties of cancer there is a tendency for the secondary growths to repeat the characters of the primary one. This is most marked in epithelioma. This, in reproducing itself, invariably maintains its primary characters. In scirrhus, the secondary growths in internal organs are usually more rapidly developed than the primary tumour; they are consequently softer and more vascular, and by those who make a distinction between scirrhus and encephaloid, they would be regarded as belonging to the latter variety of cancer.

CHAPTER XXII.

THE MYOMATA, NEUROMATA, AND ANGIOMATA.

THE MYOMATA.

The myomata are tumours consisting of muscular tissue. A new formation of muscle has been already described as being frequently associated with the ordinary process of hypertrophy, both of striated and of nonstriated muscle —a simple hyperplasia of the elements of the muscle accompanying the increase in their size. (See "Hypertrophy.")

Structure.—The myomata consist either of striated or of non-striated muscle. The former are exceedingly rare, only two or three examples having been recorded, and these were congenital.

The myomata of *non-striated* muscle consist, like the physiological tissue, of elongated spindle-shaped cells, more or less isolated or grouped into fasciculi of various sizes, with a varying quantity of connective tissue. The connective tissue is often exceedingly abundant, so much so, that these growths in the uterus—where they most frequently occur—are usually known as *fibroid tumours.* It is often necessary to macerate the tissue in dilute nitric acid in order to display the muscular elements, which by this means become isolated. The muscular fasciculi either present a regular arrangement, or pass in different directions through the tumour. The blood-vessels are distributed in the connective tissue.

DEVELOPMENT.—The myomata probably always originate from muscle, they are therefore homologous growths. In their growth they may become distinctly circumscribed tumours, but more commonly they remain as ill-defined irregular masses in the midst of the muscular tissue in which they grow. They not infrequently become pedunculated and form polypi, especially in the uterus.

SECONDARY CHANGES.—Of these, the most frequent is calcification. Hæmorrhage, mucoid softening, and the formation of cysts, are also occasionally met with.

The *uterus* is by far the most frequent seat of the myomata, and they constitute here a variety of the so-called *fibroid* tumour of the uterus. Many of these uterine fibroid tumours consist almost entirely of connective tissue, and to such the application of the term "*fibroid*" would appear to be correct. In others, however, the muscular elements form so large a proportion of the tumour that it is more properly regarded as a muscular growth. They form either distinctly circumscribed tumours, or irregular ill-defined masses in the uterine walls. Sometimes they project in the form of polypi into the uterine or abdominal cavities. Myomata may also occur in the prostate gland, in the œsophagus, and in the stomach and intestines. In the latter situations they often become pedunculated.

CLINICAL CHARACTERS.—Clinically, the myomata are perfectly innocent.

THE NEUROMATA.

The neuromata are tumours consisting almost entirely of nerve-tissue. The term "neuroma" has been applied to many growths found in connexion with nerves:—fibrous and gummy tumours growing within the nerve-sheath, and many myomata, have been included under this head.

True neuroma, however, is very rarely met with, and is amongst the least frequent of all the new formations.

STRUCTURE.—Nerve-tissue presents itself in two forms—the grey or medullary tissue, which consists principally of nerve-cells; and the white tissue, which consists of the tubular nerve-fibres. New formations of medullary tissue have been described by Virchow in the nervous centres, as local or general hyperplasias of the grey matter, but they are so exceedingly rare that a further description of them will be unnecessary. It is as a new growth of *nerve-fibres* that the neuromata are most frequently met with. They resemble in structure the cerebro-spinal nerves, consisting of tubular fibres with a varying quantity of intertubular connective tissue, and in some cases a few grey gelatinous fibres.

DEVELOPMENT.—The neuromata always originate from pre-existing nerve-tissue,—either from the cranial or from the spinal nerves. Their growth is slow, they rarely attain a large size, but usually exist as small, single nodules.

The most frequent seat of these growths is the extremities of divided nerves, where they are sometimes found after amputations. They exist, in this situation, as spherical or elongated enlargements of the divided extremity of the nerve; and they are usually intimately connected with the cicatricial tissue of the stump, from which they can only with difficulty be isolated. They may also occur in the course of the nerves in any situation, either as single or multiple nodules.

CLINICAL CHARACTERS.—Clinically, the neuromata are for the most part perfectly innocent tumours. They are said, however, to have recurred locally after removal. They always cause considerable pain.

THE ANGIOMATA.

The angiomata, or vascular tumours, are tumours consisting of blood-vessels held together by a small amount of connective tissue. They include the various forms of nævi, the erectile tumours, and aneurism by anastomosis. They may be divided into two classes—the *simple* angiomata, in which the new vessels resemble normal arteries, veins, or capillaries; and the *cavernous* angiomata, in which the blood circulates in a cavernous structure similar to that of the corpus cavernosum penis.

SIMPLE ANGIOMATA.—These include the various forms of nævi, and telangiectasis. They consist of tortuous and dilated blood-vessels, held together by a small quantity of connective and adipose tissue. The vessels are most of them of new formation; some, however, may be the original vessels of the part which have become considerably enlarged. They most commonly partake of the nature of capillaries, but in other cases the arterial or venous characters predominate. These growths are usually small, superficial, slightly elevated masses; although they sometimes form larger tumours. Their colour is red, violet, or purple, according to the character of the blood which they contain. The former is much the most frequent.

CAVERNOUS ANGIOMATA.—These include the venous vascular tumours, erectile tumours, and aneurism by anastomosis. They consist of an erectile cavernous tissue, closely resembling that of the corpus cavernosum penis. The growth is made up of irregular fibrous alveoli, which communicate freely with one another, and are lined with an endothelium similar to that of the veins. These spaces are distended with blood, usually venous, which is supplied to them by numerous tortuous vessels, and circulates in them with varying degrees of rapidity. These growths are commonly of a bluish colour. They may be diffuse, or form distinctly circumscribed tumours. They often exhibit distinct pulsation. Their favourite seat is the skin and subcutaneous tissue. They may also occur in the orbit, in muscle, and in the liver, spleen, and kidneys.

CHAPTER XXIII.

CYSTS.

IN addition to the new growths already described, there is a large class of formations, many of which cannot be regarded as "tumours" in the strict application of this term. These are the *cysts* or *cystic tumours*.

A *cyst* is a cavity containing liquid or pultaceous material, which is separated from the surrounding structures by a more or less distinct capsule. It may be a new formation, or a pre-existing structure which has become distended by its own secretion, or by extravasation into it. The former, only, comes within the category of new growths, although for the sake of convenience, it will be advisable to consider them both under one head.

There are thus two principal modes by which cysts originate—one, the most frequent, by the gradual accumulation of substances within the cavities of pre-existing structures, which are, for the most part, products of their own formation, being in some cases a secretion, and in others a cell-growth; the other, by the independent formation of a cyst in the tissues.

The accumulation of secretions and of other products within pre-existing cavities, may be effected in the three following ways:—

1st. By the retention of the normal secretion owing to the closure of the excretory ducts—as so often occurs in sebaceous glands.

2nd. By excessive secretion, the cavity being unprovided with an excretory duct—as in the formation of bursæ.

3rd. By the extravasation of blood into the cavity—as in hæmatocele.

The independent formation of a cyst may take place—

1st. By the softening and liquefaction of the tissues in some particular part, owing to mucoid or fatty changes. The tissues around the softened matters become condensed, and ultimately form a kind of cyst-wall.

2nd. By the enlargement and fusion of the spaces in connective tissue, and the accumulation of fluids within them. The surrounding tissue becomes condensed, and forms a cyst-wall; and this may, in some cases, become lined with secreting cells.

3rd. By the formation of a cyst-wall around foreign bodies, parasites, or extravasated blood.

STRUCTURE.—The wall of the cyst will vary in its nature according as it is a pre-existing or a newly-formed tissue. In the former case, it will possess an epithelial lining which will present the same characters as that of the gland, serous membrane, or other structure, from which the cyst originated. If the cyst is a new growth, it rarely possesses an epithelial lining, but consists simply of a fibrous capsule. The cyst-wall is sometimes firmly connected with the adjacent parts, so that it can only with difficulty be separated; in other cases, the union is much less intimate. Instead of being a distinct structure, it may be simply the surrounding tissue which has become dense and fibrous in character.

The contents of cysts are very various, and may serve as a basis for their classification. In the retention-cysts, they will vary with the nature of the normal secretion—serum, sebaceous matter, saliva, milk, seminal fluid, and other substances are thus found in these cysts, more or *less altered in character* from being retained in a closed cavity. In the exudation-cysts, serum is the most frequent constituent; and in extravasation-cysts, blood. In those cysts which originate from the softening and breaking down of tissue, the contents are the products of retrogressive tissue-metamorphosis, and usually consist largely of mucin, fatty matters, and serum.

SECONDARY CHANGES.—These may take place in the wall of the cyst, or in its contents. The cyst-wall itself may become the seat of new growths, and produce secondary cysts, villous, glandular, and other structures:—this occurs in many compound ovarian cysts. It may also be the seat of an inflammatory process, which terminates in suppuration and granulation, and by this means the cyst frequently becomes obliterated, its contents being either absorbed or discharged externally, and the cavity closing by granulation. Calcification and ossification of the wall may also occur. The contents of cysts undergo various changes, owing to their retention in a closed cavity. The secretions become altered in character, thickened and viscid. Epithelial elements undergo fatty changes, and so give rise to cholesterin crystals. Calcification of the contents is also common.

Cysts may be *simple* or *compound*. A simple cyst consists of a single loculus. A compound or multilocular cyst is one consisting of numerous loculi, which either communicate with one another, or remain isolated. Another variety of compound cyst, consists of a cyst with endogenous growths, the larger cyst having others growing from its walls. A compound cyst may become a simple one by the destruction of its walls.

Cysts are frequently associated with other growths, hence the terms—"cystic-sarcoma," "cystic-cancer," &c. It is especially in those growths which originate in glandular structures, as in the mamma, testicle, and ovary, that this combination is met with. The cystic development may almost entirely obliterate the structure of the mour in which it takes place, so that ultimately the tter becomes converted into a combination of cysts. ı other cases large portions of the tumour grow into ıe cystic cavities. Considerable difficulty is thus not ıfrequently caused in determining the nature of the iginal growth.

CLASSIFICATION.—Cysts may be most conveniently classified according to their mode of origin, thus:—

CLASSIFICATION OF CYSTS.

I. *Cysts formed by the accumulation of substances within the cavities of pre-existing structures.*

- A. RETENTION CYSTS.—Cysts resulting from the retention of normal secretions. These include—
    - α. *Sebaceous Cysts.*—These are formed by the retention of secretions in the sebaceous glands. Such are comedones and atheromatous tumours.
    - β. *Mucous Cysts.*—These are formed by the retention of secretions in the glands of mucous membranes.
    - γ. *Cysts from the retention of secretions in other parts*, including—Ranula, from occlusion of the salivary ducts; Encysted Hydrocele, from occlusion of the tubuli testis; cysts in the mammary gland, from obstruction of the lacteal ducts; simple, and some compound cysts of the ovary, from dilatation of the Graafian follicles; and simple cysts of the liver and kidneys.
- B. EXUDATION CYSTS.—Cysts resulting from excessive secretion in cavities unprovided with an excretory duct. These include Bursæ, Ganglia, Hydrocele, and many cysts in the broad ligament.

C. **Extravasation Cysts.**—Cysts resulting from extravasation into closed cavities. These include Hæmatocele, and some other forms of sanguineous cysts.

II. *Cysts of independent origin.*

A. **Cysts from Softening of Tissues.**—These are especially common in new formations, as in enchondroma, lipoma, sarcoma, &c.

B. **Cysts from Expansion and Fusion of Spaces in Connective Tissue.**—These include—

a. *Bursæ,* originating from irritation and exudation into the tissues.

β. *Serous cysts in the neck* (often congenital).

γ. *Many compound ovarian cysts.*[*]

C. **Cysts formed around Foreign Bodies, Extravasated Blood, and Parasites.**

D. **Congenital Cysts.**—These include many Dermoid cysts. These appear often to be the remains of blighted ova. They contain fatty matters, hair, teeth, bones, &c.

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[*] See Dr. Wilson Fox, on Cystic Tumours of the Ovary, "Med. Chir. Soc. Trans.," vol. xlvii.

CHAPTER XXIV.

INFLAMMATION.

The morbid processes which have thus far been described, have been mainly characterized by some alteration in the normal nutrition of the histological elements; either by a diminution in their nutritive activity—as in atrophy and the degenerations, or by an increase—as in hypertrophy and the new formations. In the process of *inflammation*, an alteration in nutrition also plays a prominent part, but changes in the blood-vessels and in the circulation are its essential and most important constituents.*

Inflammation is the succession of changes which takes place in a tissue as the result of some kind of injury, provided that this injury be insufficient immediately to destroy its vitality. With regard to the nature of the injury—it may consist in some *direct* irritation of the tissue, either by mechanical or chemical agents, or by substances conveyed to it by means of the blood-vessels or lymphatics; or in an *indirect* irritation, as in some cases of inflammation of internal organs arising from exposure to cold. In all cases, however, some injurious stimulation of the tissue precedes the occurrence of the local changes which constitute the inflammatory process.

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* With regard to the general pathology of Inflammation, the reader is especially referred to the works of Virchow, Cohnheim, Stricker, and Burdon-Sanderson. The most able article by Professor Sanderson, in *the fifth volume* of "Holmes's System of Surgery," *contains an admirable* exposition of what is known on the subject.

The exact nature of these changes has, for the most part, been ascertained during the past six years, mainly owing to the experimental researches of Professors Cohnheim, Stricker, and Burdon-Sanderson. The method of investigation has consisted in the artificial production of inflammation in the lower animals, and the observation of the process as thus induced. The process comprises—

1st. *Changes in the blood-vessels and circulation.*

2nd. *Exudation of liquor sanguinis and migration of white blood-corpuscles;* and

3rd. *Alterations in the nutrition of the inflamed tissue.*

It will be well, in the first place, to consider each of these separately, in the order in which they occur, and subsequently to endeavour to point out how far a causal relation exists between them.

I. CHANGES IN THE BLOOD-VESSELS AND CIRCULATION.—Changes in the blood-vessels and circulation, resulting in increased vascularity, have ever been regarded as playing a most important part in inflammation, as upon them principally depend those signs of the process which are most obvious during life. The redness, heat, and swelling, which are so constantly met with in inflamed tissues, are in great measure due to the attendant hyperæmia. The swelling, however, is in most cases dependent rather upon the effusion and cell-growth, than upon the overfulness of the blood-vessels.

These changes in the blood-vessels and circulation are essential constituents of inflammation, both in vascular and in non-vascular tissues. In the latter, which comprise the cornea and cartilage, they take place in the adjacent vessels from which these tissues derive their nutritive supply. The nature of these vascular changes has been studied by the artificial production of inflammation in transparent tissues, in which the circulation can be readily observed; the web and mesentery of the frog, and the wing of the bat, being most convenient for this purpose. The phenomena, as observed in the mesentery of the frog, may be thus briefly described:—

The first effect of irritation of the mesentery—mere exposure to the air being sufficient for the purpose—is to cause *dilatation* of the arteries, and after some interval, a similar dilatation of the veins. The dilatation of the arteries commences at once, and is not preceded by any contraction. It gradually increases for about twelve hours, and is accompanied also by an increase in the length of the vessels, so that they became more or less tortuous. This enlargement of the blood-vessels is associated at the commencement of the process with an *acceleration* in the flow of blood; this, however, is soon followed by a considerable *retardation* in the circulation, the vessels still remaining dilated. These alterations in the rapidity of the blood-flow cannot be owing to the increase in the calibre of the vessels, which remain throughout dilated. The relation which subsists between the two phenomena is unknown.

The retardation of the circulation usually commences somewhat suddenly, and is first observable in the veins. The rapidity of the current varies, however, in different vessels. In some—both arteries and veins—it may be more rapid, in others, very slow, oscillating to and fro, or even completely stagnant; these differences occurring perhaps in contiguous vessels, without any obvious cause. The capillaries and small arteries often present at the same time numerous irregular bulgings and contractions; in many parts they may be distinctly aneurismal and varicose.

As the circulation becomes slower, the white blood-corpuscles (leucocytes) accumulate in the veins. Their *natural tendency to* adhere to the sides of the vessel is increased, so that they may nearly fill the tube. At the same time they exhibit active movements, by means of which they penetrate the walls of the vessels and pass into the surrounding tissues. This phenomenon will be described under the head of "Exudation of Liquor Sanguinis and Migration of White Blood-Corpuscles." The absolute number of white blood-corpuscles may also be increased owing to the irritation of the lymphatic structures in the vicinity of the inflamed tissue.

Stasis.—The gradual diminution in the rapidity of the circulation and the accumulation of the blood-corpuscles in the vessels may be ultimately followed by the complete stagnation of the current, constituting the condition long known as *inflammatory stasis.* When this has occurred, the red corpuscles which have accumulated in the capillaries are seen to adhere to one another and to the sides of the vessels, and they may become so closely packed that their outlines can scarcely be distinguished.

II. EXUDATION OF LIQUOR SANGUINIS AND MIGRATION OF WHITE BLOOD-CORPUSCLES. — Another constituent of the inflammatory process consists in the exudation of the liquor sanguinis and the migration of the white blood-corpuscles.

a. Migration of White Blood-Corpuscles.—The migration of white blood-corpuscles (leucocytes) through the walls of the blood-vessels was first described, although very incompletely, by Dr. W. Addison in 1842.* This observer stated as the result of his researches, that in inflammation these corpuscles adhered to the walls of the vessels and passed through them into the surrounding tissues. In 1846 Dr. Augustus Waller described more fully the same phenomenon, and from his description there can be little doubt that he actually observed the emigration of the corpuscles.* Both these observers concluded that the escaped blood-corpuscles became pus-corpuscles. Their observations, however, were but little thought of and were soon forgotten, and it was not until 1867, when similar investigations were instituted quite independently by Professor Cohnheim, of Berlin—to whose minute researches we must ascribe most of our present knowledge on this subject—that the emigration of blood-corpuscles came to occupy an important place in the pathology of inflammation.

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* "Experimental and Practical Researches on Inflammation," *Trans. Prov. Med. Association*, 1842.

The emigration may be observed in the mesentery of a frog which has previously been paralysed by the subcutaneous injection of curare. The changes in the blood-vessels and in the circulation, and the accumulation of blood-corpuscles in the part, have been already described; it remains only to consider the phenomena of emigration.

The white blood-corpuscles (leucocytes) which have accumulated in large numbers, especially in the veins, remain almost stationary against the walls of the vessel, the blood-current passing by them, although with much diminished velocity. Those immediately adjacent to the wall, gradually sink into it, and pass through it into the surrounding tissue. In doing so they may be observed in the various stages of their passage. At first small button-shaped elevations are seen springing from the outer wall of the vessel. These gradually increase until they assume the form of pear-shaped bodies, which still adhere by their small ends to the vascular wall. Ultimately the small pedicle of protoplasm by which they are attached gives way and the passage is complete, the corpuscle remaining free outside the vessel.

In explanation of this phenomenon—there can be no doubt that the passage of the corpuscles is effected by virtue of their own amœboid activity, by means of which they penetrate the walls of the vessels. The capillaries are now known to consist of protoplasm, and hence the penetration of their contractile walls by the amœboid corpuscles, and the subsequent closure of the openings when the transit is completed, can be readily understood. The corpuscles having escaped from the vessels into the surrounding tissues, continue to exhibit active movements. They may multiply by division, and thus rapidly increase in number: this will be again referred to when speaking of the origin of pus.

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* *Phil. Magazine*, vol. xxix. 1846.

Not only is there an emigration of white blood-corpuscles in inflammation, but the red corpuscles also pass through the walls of the blood-vessels, though in much less considerable numbers; and their transit is mainly through the walls of the capillaries. This passage of the red corpuscles takes place in simple mechanical congestion, it may be observed in the web of a frog in which the circulation has been artificially arrested by ligature of the femoral vein. (See "Mechanical Hyperæmia.")

β. Exudation of Liquor Sanguinis.—Associated with the passage of the blood-corpuscles through the walls of the vessels, is an exudation of the liquor sanguinis. The exuded liquor sanguinis—which constitutes the well-known *inflammatory effusion*—differs from the liquid which transudes as the result of simple mechanical congestion, inasmuch as it usually contains a larger proportion of albumen and fibrinogenous substance, a proportion which increases with the intensity of the inflammation. It also contains an excess of phosphates and carbonates.

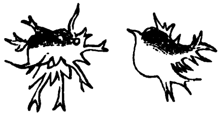
The most characteristic feature of inflammatory effusion is the large number of cell-structures which it contains. These are the direct product of the inflamed tissue, and are in no case generated spontaneously in the effused liquid. Most of them are migrated blood-corpuscles, others are derived from the proliferating elements of the tissue. The quantity and nature of the effusion will thus vary with the tissue inflamed, and with the severity of the inflammatory process. In non-vascular tissues, as cartilage and the cornea, exudation can only occur to a small extent from the neighbouring vessels, and hence the effusion is small in quantity. In dense organs, as the liver and kidney, owing to the compactness of the structure, a large amount of effusion is impossible, and what there is, is so intermingled with the structural elements of the organ that it does not appear as an independent material. In the kidney it escapes into the urinary tubes and so appears in the urine. The effusion is most abundant, and constitutes an important *visible* constituent of the inflammatory process, in inflammation of those organs which possess a lax structure and in which the vessels are but little supported—as the lungs, and in tissues which present a free surface—as mucous and serous membranes.

III. Alterations in the Nutrition of the inflamed Tissue.—The remaining constituent of the inflammatory process consists in an alteration in the nutrition of the elements of the inflamed tissue. The nutritive changes, although they may differ according to the structure of the part, are all characterized by an *increase* in the nutritive activity of the cellular elements.

The nature of these nutritive changes has for the most part been ascertained by the investigation of tissues in the lower animals, in which inflammation has been artificially induced. In man, the study of the primary lesions is difficult, owing to the fact that the process can rarely be observed in its earlier stages. These changes will be more fully described when considering inflammations of particular organs and tissues; it will be sufficient in the present place merely to indicate their general characters.

The alteration in nutrition, as already stated, is characterized by an exaltation of the nutritive functions of the cellular elements of the tissues involved in the inflammatory process. This is evidenced by an increase in the activity of those elements which normally exhibit active movements, as the amœboid cells of connective tissue and of the cornea. Cells, which under normal circumstances undergo no alterations in form and exhibit no active movements, become active—sending out processes, and undergoing various alterations in shape. (Fig. 46.) This increase in the activity, and variation in the form of the cells, is usually accompanied by the growth of their protoplasm, and frequently by its division, and thus by the formation of new cells. In many cases the protoplasm, as it increases in bulk, becomes cloudy and granular, so much so as frequently to completely obscure any nuclei which it may contain. This occurs especially in epithelial elements, and it constitutes the condition known as "*cloudy swelling.*" It is well seen in the glandular epithelium of the kidney in acute tubal nephritis. (See Figs. 75, 76.) The granules are readily distinguishable from fatty particles, inasmuch as they are quickly dissolved by dilute acetic acid.

FIG. 46.



Amœboid Leucocytes. (v. Recklinghausen.)

This increased activity of the cellular elements varies considerably in different tissues, and even in the elements of the same tissue. Some cells exhibit active movements and form new cells much more readily than others. *Those tissues*, for example, which naturally maintain *themselves* by the multiplication of their elements, as the epithelial tissues, become active very readily in inflammation, very slight degrees of irritation being sufficient to cause in them rapid cell-proliferation. This is seen in inflammation of mucous membranes, and of the epidermis. In tissues, on the other hand, whose elements normally exhibit no tendency to multiplication, as cartilage, active changes are much less readily induced, the cells are much more stable and multiply with far less facility, and if the inflammation is slight, they may not multiply at all but simply become enlarged and undergo some alteration in form. Lastly, in the higher tissues, the stability of the elements reaches its maximum, and in nerve-cells no increase of activity can be induced.

Different cells in the same tissue exhibit also different degrees of stability. In common connective tissue and the cornea, for example, the amœboid cells are the least stable, and are the first to multiply. Possibly the age of the cells may influence their tendency to become active, the newer being less stable than the older elements.

The earliest nutritive change is thus one of cell-growth and cell-proliferation; the subsequent ones are characterized either by impairment of nutrition and the degeneration and death of the newly-formed elements, or by the development of these into a permanent tissue. As a rule it may be said, that the new cells are less developed than those from which they originated, much more prone to undergo retrogressive changes, and if they form a new tissue, this is inferior in its organization to that of the original structure. If the inflammatory process be of considerable severity and stasis be induced in a wide area of the tissue, the nutrition may become completely arrested and gangrene be the ultimate result. (See "Causes of Gangrene.") The tendency of the new elements to undergo progressive development will vary with the tissue involved, and with the intensity of the inflammation. *The more intense* the inflammation, the more abortive are the young cells, and the less is their tendency to form a permanent tissue. (See "Acute and Chronic Inflammations.")

In connective tissues, these changes in the cells are necessarily accompanied by changes in the intercellular substance. The latter are for the most part characterized by softening. In common connective tissue, the fibres in the first place become succulent and less distinct, and ultimately they are completely destroyed; in cartilage, the matrix softens and liquefies; in bone, the lime-salts are removed, the lamellæ disappear, and the osseous structure becomes converted into medullary tissue. Hence the destructive effects of the inflammatory process.

Having thus briefly described the succession of changes which occurs in the process of inflammation, it remains to consider in what way these result from the injurious stimulation of the tissue, and how far a causal relation subsists between them.*

The first apparent change which follows the irritation of the tissue, consists in the dilatation of the blood-vessels and in an *acceleration* of the flow of blood. Respecting the cause of this primary vascular phenomenon—recent physiological investigations show that a similar dilatation of the vessels and increase in the activity of the circulation is produced by the excitation of a sensory nerve in those parts in which the nerve originates; and it must be regarded as in the highest degree probable, that the primary vascular phenomena in inflammation are in the same way owing to an injurious impression received by the sensory nerves being reflected by the vaso-motor centre to the vessels. How such an excitation of the nerve produces dilatation of the vessels and increased rapidity of the circulation is, however, unknown.

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* *The* following conclusions are in the main those arrived at by *Professors* Stricker and Burdon-Sanderson.—*Holmes's System of Surgery*, vol. v.

With regard to the cause of the *retardation* of the blood-stream which so quickly succeeds its acceleration, and which may ultimately terminate in complete stasis—the observations of Professor Lister and Dr. Ryneck tend to show that it consists in some alteration in the properties of the *walls of the blood-vessels* through which the blood passes, and not in changes in the blood itself. The accumulation of the red blood-corpuscles in the inflamed part, and their adhesion to one another and to the walls of the blood-vessels (see "Stasis"), Professor Lister considers to be owing to their natural tendency to cohere together when in abnormal circumstances, such as often occurs after their removal from the body; and he says that this tendency is not greater in the blood of inflamed tissues than in normal blood.[*] He also finds that the aggregation is as marked in blood which has been defibrinated. These observations seem to point to some alteration in the walls of the vessels as the cause of the stasis, and not to any abnormal condition of the corpuscles themselves. The investigations of Dr. Ryneck tend to confirm the same view.[†] Dr. Ryneck has shown that stasis may be produced in the web of a frog, in which milk or defibrinated blood has been injected in place of the normal blood; and also that in vessels, the vitality of which has been destroyed or altered by the injection of poisonous metallic substances, no statis can be produced. These results appear to be conclusive, and show that the retardation and ultimate stagnation of the blood-stream in inflammation, are owing to some alteration in the vital properties of the walls of the blood-vessels with which the circulating blood comes into contact.

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[*] "On the Early Stages of Inflammation."—*Philosoph. Trans.* 1858.

[†] Ryneck, "Zur Kenntniss der Stase des Blutes in den Gefässen Entzündeter *Theile.*"—Rollet's *Untersuch. aus dem Institute für Phys. u. Histol. in Graz.*

The exudation of liquor sanguinis and migration of white blood-corpuscles, which take place coincidently with the retardation of the blood-stream, are so closely associated with it, that they must be regarded as being dependent upon the same cause. The walls of the blood-vessels appear to become so altered, that they not only cause stagnation of the circulation, but at the same time permit the liquor sanguinis to transude with abnormal facility, and the white blood-corpuscles to penetrate them.

The remaining constituent of the inflammatory process —the alteration in the nutrition of the inflamed tissue— succeeds the changes in the circulation and the exudation. Respecting the cause of the increased nutritive activity of the cellular elements which characterizes this tissue-change—it is probable that it is for the most part the result of the stimulation of the cells by the liquor sanguinis exuded from the blood-vessels. This conclusion is mainly based upon the well-known experiment of Professor Stricker, which consists in the excision of the cornea of a frog, and its insertion beneath the membrana nictitans of the opposite eye, in which inflammation has been previously induced. The transplanted cornea, when removed in the course of twenty-four hours, exhibits all the anatomical inflammatory changes observed in the unexcised cornea of the opposite eye. Hence Stricker concludes that the structural changes in inflammation of the cornea of the frog are owing to the stimulation of its elements by the liquid exuded from the blood-vessels, and are quite independent of nervous influence. That the increased nutritive activity of the elements of the inflamed tissue is, however, in *every inflammatory* process the result of their stimulation *by the* exuded liquor sanguinis, cannot be regarded as by any means certain. It is possible that the cellular elements may be stimulated to increased activity by means of impressions conveyed to them through the nervous system, and also that an irritation received by one element may be transmitted to another. This latter hypothesis, however, is not a probable one.

SUPPURATION.—Suppuration, and the formation of abscesses, is a very frequent result of the inflammatory process; it occurs much more frequently, however, in some inflammations than in others. As a rule it may be stated that the more intense the inflammation the more abundant is the formation of pus.

The essential constituents of pus are cells and a liquid in which they are suspended. The liquid closely resembles the liquor sanguinis. It contains albumen, pyin, chondrin, fatty matters, and inorganic substances. The cells, or *pus-corpuscles* (leucocytes) are indistinguishable from the white corpuscles of the blood. They are spherical, spheroidal, or irregular shaped semi-transparent bodies, from $\frac{1}{2500}$ to $\frac{1}{3500}$ of an inch in diameter, containing a varying number of granules, and usually one or more distinct nuclei. (Fig. 47.) The addition of dilute acetic acid causes the cells to swell up; they become more spherical and transparent, and the nuclei are rendered more apparent. The size of the corpuscles and nuclei, and the number of the granules, present manifold variations. *Pus-corpuscles,* like white blood-corpuscles, lymph-

FIG. 47.

Pus-corpuscles as seen after death. *a.* Before, *b.* after, the addition of dilute acetic acid. × 400.

corpuscles, and many other young cell-forms—all of which are included under the common term of "*leucocytes*"—are masses of contractile protoplasm. They possess the power of spontaneous movement, and may undergo continuous alterations in form, or migrate in the tissues. (See Fig. 46.) They may also multiply by division.

The mode of origin of pus has lately been the subject of much controversy. The liquid ingredient proceeds directly or indirectly from the blood, it is the exuded liquor sanguinis: about this there is no dispute. The difference of opinion which exists is respecting the origin of the formed elements. Without discussing the theories which have been advanced by different pathologists, it must now be admitted that there are at least *two* sources from which the corpuscles of pus may be derived—one from the *blood*, and the other from the *inflamed tissues.*

It has been seen that in the process of inflammation, innumerable white blood-corpuscles pass out of the vessels into the surrounding tissues, and as these are indistinguishable from pus-corpuscles, it must be conceded that one mode of origin of pus is from the blood. Further, the white blood-corpuscles may multiply by division, and thus it is probable that by this means the production of pus is greatly increased.

The other source from which the corpuscles of pus are derived, is from the cellular elements of the inflamed tissue. These, as has been described, are the seat of active changes in inflammation; they may multiply and form new cells, and the more intense the inflammation, the more lowly organized are the newly formed elements, and the less is their tendency to form a permanent tissue. Some of these newly formed cells constitute pus-corpuscles. These, in this case must be regarded as young elements resulting from the proliferation of the tissue, which are of low vitality, and soon perish. Pus-corpuscles may probably originate in this way, from the proliferation of any tissue with the exception of nerve, either by simple division or by endogenous multiplication.

Although the formed elements of pus may thus be derived both from the blood and from the inflamed tissue, there can be no doubt that the former is their principal source, and that they are in the main migrated blood-corpuscles. In the earlier stages of the inflammatory process, they are mostly, if not all, emigrants; but in the later stages it must be admitted that they may also be derived from the cells of the inflamed tissue.

Such being the modes of origin of pus, it is evident that the more abundant the escape of blood-corpuscles, and the more active the proliferation of the elements of the inflamed tissue, the greater will be the formation of pus, and hence the greater its tendency to collect so as to form abscesses. It is consequently in those inflammations which are the most *concentrated* and the most *intense*—provided that the injury is not sufficiently severe to cause instantaneous stasis—that the formation of pus is most abundant. The greater the injury sustained by the walls of the blood-vessels, the more readily will the blood-corpuscles penetrate them, and hence the more abundant will be the formation of pus. In inflammations of less intensity the escape of blood-corpuscles is less abundant, and the proliferation of the tissue less active, so that pus is not produced in sufficient quantities to cause its collection in the form of an abscess.

Pus exercises a most injurious influence upon the surrounding tissues. The pus-corpuscles appear to be endowed with the power of absorbing the tissues with which they come in contact, or, at all events, of causing their liquefaction. Hence the softening and disintegration of the tissues which constitute such a destructive element in intense inflammations.

Pus which has remained for any length of time in the *tissues undergoes certain* changes; thus its elements may undergo fatty metamorphosis, and thus be rendered capable of absorption. If the pus is confined in a closed cavity, its liquid portions become absorbed, its cells atrophy, and it may gradually dry up into a caseous mass, which may subsequently become calcified.

VARIETIES OF INFLAMMATION.—Inflammation exhibits certain variations in its characters according to the *severity* of the irritation which produces it. The more severe the irritation upon which the inflammatory process depends, the greater will be the damage sustained by the blood-vessels, and consequently—if instantaneous stasis be not produced—the greater will be the tendency to the exudation of liquor sanguinis and to the emigration of leucocytes. Hence it is in inflammations of considerable severity that the vascular phenomena are often so pronounced, the formation of pus so abundant, and the softening and disintegration of the tissues so considerable. Such inflammations, inasmuch as the action of the irritant which produces them is for the most part of short duration, are sometimes designated *acute inflammations.*

In inflammations of less intensity, in which the damage sustained by the blood-vessels is less severe, the textural changes occupy a more prominent place, whereas the vascular phenomena are usually much less marked, and the formation of pus is less abundant. The precise nature of these textural changes must obviously partly depend upon the characters of the tissue which is the seat of the inflammation, but variations are also produced according to the severity of the irritating agent. It appears to the author to be probably true—that the less severe the irritant which produces the inflammation, the more do the resulting textural changes tend to be limited to the *connective tissue which is immediately adjacent to the blood-vessels and lymphatics;* whereas in inflammations of somewhat greater intensity more distant elements become involved. This is seen, for example, in inflammatory processes in the kidneys and in mucous membranes. In the former, the least severe forms of inflammation are characterized anatomically by an increase in the connective tissue around the blood-vessels (see "Interstitial Nephritis"); whilst in inflammations of presumably somewhat greater intensity, the prominent textural change consists in swelling or proliferation of the epithelium within the tubules (see "Tubal Nephritis"). In mucous membranes also, the more severe inflammations are attended by epithelial proliferation, the less intense and more chronic by changes in the submucous connective tissue. With regard to the cellular elements in which these active changes take place—they are probably those which are the most intimately connected with the lymphatic system—viz., the cells of the connective tissue, and the endothelium of the lymphatics and of the blood-vessels. The tendency of the textural changes resulting from the least severe forms of inflammation to be limited to the connective tissue immediately adjacent to the blood-vessels and lymphatics, gives to these inflammations certain peculiarities. The new tissue originating around the vessels—consisting in the earlier stages mainly of small round cells, but ultimately becoming developed into a more or less completely fibrillated structure—leads to an *induration* of the organ in which it is situated, and very constantly, to the subsequent atrophy and retrogressive metamorphosis of its other histological elements. These changes will be more fully considered when treating of inflammation of the individual organs and tissues. (See "Inflammation of Common Connective Tissue," "Cirrhosis of the Liver," &c.) These least severe forms of inflammation, inasmuch as the irritant which produces them is not only of slight severity but is usually also prolonged in the duration of its action, are often known as *chronic inflammations.*

Inflammations have received different names according to the *nature* of the injury upon which they depend. Those inflammations which result from external injuries, mechanical or chemical violence, are called *traumatic.* In those cases in which the injurious stimulation of the tissue is owing to the transmission of infective materials by means of the blood-vessels or lymphatics from some local infecting centre, as in pyæmia and acute miliary tuberculosis, the resulting inflammations are called *infective.* Inflammations in which the nature of the injury is not obvious, are usually called *idiopathic.* Lastly, the nature of the injury may give to the inflammatory process certain peculiarities. The contagium of small-pox, for example, gives rise to inflammation of the skin, constituting the "rash"; that of syphilis, to certain inflammations of the skin, mucous membranes, and other tissues; and that of typhoid fever, to inflammation of the intestinal lymphatic structures. In all these and numerous similar cases, the nature of the irritant impresses upon the inflammation certain peculiarities, and in so far as the former is specific, the latter may be called *specific* inflammations.

Of these different varieties of inflammation, the infective inflammations, including pyæmia and acute tuberculosis, and the specific inflammations resulting from the poison of syphilis, will be separately considered in the next following chapters. The pathology of inflammation will then be still further elucidated by the study of the process as it occurs in the various tissues and organs.

CHAPTER XXV.

ACUTE TUBERCULOSIS.

By acute tuberculosis is understood a general infective disease, which is characterized anatomically by the occurrence of numerous minute nodular lesions more or less generally disseminated in the various organs and tissues. The generally disseminated nodular lesions, which are characteristic of the disease, appear to be inflammatory growths, resulting from the distribution of infective materials (probably minute particles) by means of the blood-vessels or lymphatics from some primary inflammatory product. They are, therefore, the anatomical results of an infective inflammatory process, and they constitute what have long been known as *miliary tubercles*.

Our knowledge of acute tuberculosis and of its anatomical result—*tubercle*, has until quite recently been involved in obscurity; but at the present time—owing in great measure to scientific experimental research—it may be regarded as being tolerably complete. According to the older doctrines, which were based upon the teaching of Laennec, tubercle was looked upon as a specific non-inflammatory growth which originated spontaneously in the tissues. Further, this new growth was characterized by the regular succession of changes which it invariably underwent:—it was first grey and translucent, then became opaque, and ultimately caseous. Hence in its earlier stages it was known as *grey*, in its latter, as *yellow* tubercle. Caseous metamorphosis was held to be such a distinguishing peculiarity of the growth, that all caseous masses were regarded as tubercular, and the term "tubercle" came to be applied indiscriminately to all pathological products which had undergone this form of degeneration, and which in their colour and consistence somewhat resembled soft cheese. Caseation, however, as already stated, is a common result of the retrograde metamorphosis of many growths which are destitute of or contain but few blood-vessels, and which consist of closely-crowded cellular elements; and although it may occur to a greater or less extent in tubercle, it is by no means specially characteristic of this morbid growth. (See "Caseation.") For this much wider extension of the pathological significance of caseous degeneration we are mainly indebted to Professor Virchow.

The infective nature of acute tuberculosis was first promulgated about sixteen years ago by Buhl, who stated that in the majority of cases of this disease, indurated masses which had become caseous existed in some part of the body, and that to the absorption of substances from these infective centres the general development of the tubercle was owing. He further stated that in those cases in which the tubercles were confined even to limited portions of a single organ, they were also secondary to old inflammatory lesions. This view of the pathology of the disease has since been considerably strengthened by the results which have been obtained from the artificial production of tuberculosis in the lower animals.

The experimental investigation of acute tuberculosis was commenced by Villemin, and subsequently followed out by Burdon-Sanderson, Wilson Fox, Cohnheim, Klebs, and others. The method of investigation consisted either in the inoculation of various inflammatory products—for the most part products of *chronic* inflammations—or in the production of a local inflammatory induration by the introduction of setons and of other foreign bodies beneath the skin. Of inflammatory products Dr. Sanderson found that none proved so active as that obtained from the indurated lymphatic glands of an animal already suffering from the disease. In both cases, after a certain lapse of time, disseminated inflammatory lesions were produced in various organs and tissues—lesions which presented a special tendency to become caseous at their centres. It was also found that the distribution of these lesions varied according as the infective materials were introduced into the blood-vessels or lymphatics, clearly proving that they resulted from the dissemination of infective substances by means of the blood and lymph streams. The results of these experiments therefore show that the circulation of the products of certain *chronic* inflammatory processes is followed by the occurrence of disseminated inflammatory indurations—in other words, by a general tuberculosis.

The lesions produced, however, in artificial tuberculosis differ somewhat from those met with in the natural disease as it occurs in man. In man the lesions consist for the most part of small greyish miliary nodules ("grey tubercles"), many of which tend to become fibrous, whilst others undergo retrogressive changes, and ultimately caseate in their centres. In the disease as artificially induced in the lower animals, on the other hand, although many of the lesions are miliary nodules, there are associated with these in various organs diffused tracts of consolidation, and these often constitute the more prominent structural changes. Further, the tendency to caseation is much more marked in the lesions artificially induced than in those met with in man. These differences, however, are probably to be regarded as resulting from differences in the intensity of the infective agent, and from peculiarities in the morbid tendencies of the tissues involved, and not as any evidence of a want of analogy in the pathology of the two diseases.

With regard to the source of infection in the natural disease as it occurs in man—the masses of caseous inflammatory induration which are in the great majority of cases to be found in some part of the body, must be regarded, as indicated by Buhl, as the infective centres from which the infective materials are derived and more or less universally distributed by means of the bloodvessels and lymphatics. These caseous masses are met with in various situations, sometimes in the lungs, sometimes in the bronchial glands, sometimes in the glands of the mesentery, &c. At the same time it must be admitted that in some cases of acute tuberculosis no such foci of infection are discoverable. This, however, does not appear to be sufficient to negative the view of the infective nature of the disease—a view which is supported by its clinical characters, by the general dissemination of the lesions, and by its close analogy with the processes artificially induced. Why these chronic inflammatory products should in some cases constitute active foci of infection, whilst in others they remain inert, we are unable certainly to explain. In attempting to answer this question, it must be remembered that such products may *accidentally* become placed in direct communication with the vascular or lymphatic systems; and also that infective substances are much more liable to produce results in some constitutions and in some conditions than in others.

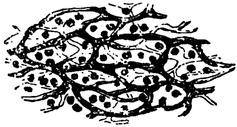
Whilst acute tuberculosis is thus an infective disease, it is an infective disease of a special kind. In the first place, the infective substances derived from the infective focus—which are probably minute particles—not only exercise their irritating influence over areas of tissue which are for the most part exceedingly small (hence the miliary character of the lesions), but the irritation they produce is of comparatively slight severity. The principal result of their irritation is consequently a textural change—a new growth of tissue at the seat of the injury. (See "Chronic Inflammations.") In this respect this disease presents a marked contrast to one with which it is closely allied—pyæmia, in which the severity of the injury produced by the infective particles is much greater and gives rise to the formation of abscesses (see "Pyæmia"). In pyæmia the intensity of the disseminated inflammatory processes is considerable and the course of the disease is usually acute, whilst in acute tuberculosis the inflammatory processes are much less severe and the disease tends to run a more chronic course.

Another characteristic of acute tuberculosis consists in the fact that the lesions appear, for the most part, to originate from elements which either belong or have a close relation to the *lymphatic system;* and that in their anatomical characters many of them somewhat resemble the follicular structure of a lymphatic gland (the "adenoid tissue" of His). The distribution of lymphatic tissue is much more general than was formerly supposed. It exists largely in the submucous tissue, around the bloodvessels in many situations, in the peribronchial tissue, beneath the endothelium of serous membranes; and in numerous other situations (see "The Lymphomata"); and from this universally distributed lymphatic tissue, as was shown by Dr. Burdon-Sanderson, most of the miliary lesions in acute tuberculosis originate.

The anatomical resemblance which exists between many of the miliary lesions and the follicular structure of a lymphatic gland is such, that when tubercle was regarded as a non-inflammatory growth it was classified by Virchow amongst the lymphomata. This resemblance, however, does not appear to be so close as has been supposed.

The miliary lesions in acute tuberculosis, although presenting certain differences according to the nature of the tissue in which they originate, are tolerably uniform in their anatomical characters. They consist, in the main, of small spheroidal elements resembling lymph-cells (lymph-corpuscles), which are either separated from one another by fine lines of homogeneous transparent-looking material, or, more commonly, by a delicate tissue which forms a more or less distinctly fibrillated network within the meshes of which the elements are grouped (Fig. 48, see also Fig. 56). This structure is very similar to that which is often met with as the result of other chronic inflammatory processes, *e.g.* in the chronic indurations of the liver, lungs, and other organs. In some of the nodules the fibrillated network is well marked, whilst in others it is almost completely absent. In addition to the small lymph-like corpuscles there are often some larger cells containing one, and in some cases, two or three nuclei. (See Fig. 35.) These larger cells resemble those so often met with in lymphatic tissues which are undergoing active growth.

FIG. 48.



A portion of a Grey Miliary Tubercle. Showing the typical structure which constitutes the greater portion of these nodules. × 200.

Although the structure above described forms the bulk of the greater number of the miliary nodules, it will be found on careful examination that they present some additional characteristics. In the first place, it is exceedingly common to distinguish several centres in the nodule around which the cellular elements are more or less concentrically grouped; this appearing to indicate the existence of separate centres of development. As many as four or five centres are sometimes to be seen in a single nodule. (See Fig. 55.)

Another feature of the miliary nodules is that when examined in certain stages of their development large multinucleated masses of protoplasm, somewhat resembling the "myeloid cells," are very frequently to be found associated with the lymph-like elements. These large multinucleated cells have been alluded to by Virchow, Wagner, and others, but it is only quite recently, owing to the researches of Dr. Oscar Schüppel, that they have received a prominent place in the pathology of tubercle. As the views of this pathologist concerning their mode of origin and on the pathology of tubercle generally differ somewhat from those commonly entertained, the author merely proposes in the present place to state very briefly the result of his own observations made subsequently to the perusal of Dr. Schüppel's valuable publications. For more complete information the reader is referred to Dr. Schüppel's writings on the subject.*

The most characteristic features of these multinucleated cells are their large size, the number of their nuclei, and the irregularity of their outline. Some of the larger ones measure, exclusive of their processes, as much as $\frac{1}{200}$ inch in diameter. They possess no limiting membrane, but many of them have long branched processes which are directly continuous with the reticulum of the tuberculous nodule. (Fig. 49; see also Fig. 51.) They contain numerous large round or roundly-oval nuclei, each enclosing

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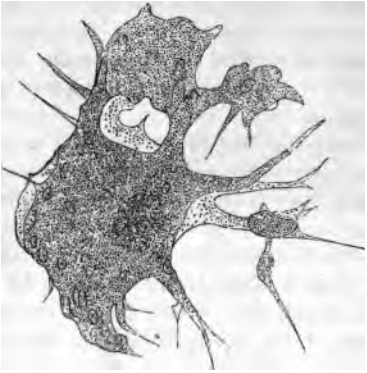
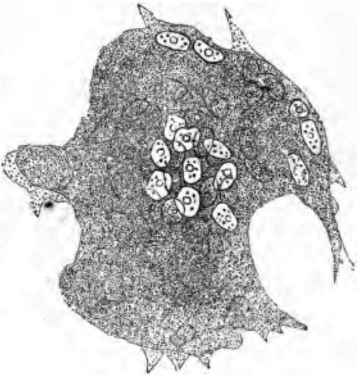
* Untersuchungen über Lymphdrüsen-Tuberkulose; Dr. Oscar Schüppel: Tübingen, 1871; and Ueber die Entstehung der Riesen*zellen im Tuberkel.—Wagner's Archiv der Heilkunde*, vol. xiii. 1872.

FIG. 49.



A Multinucleated Cell from the Lung in a case of Chronic Phthisis. Showing the long-branched processes, which are continuous with the reticulum of the surrounding indurated growth. Some of the processes are in connexion with smaller nucleated elements. × 200.

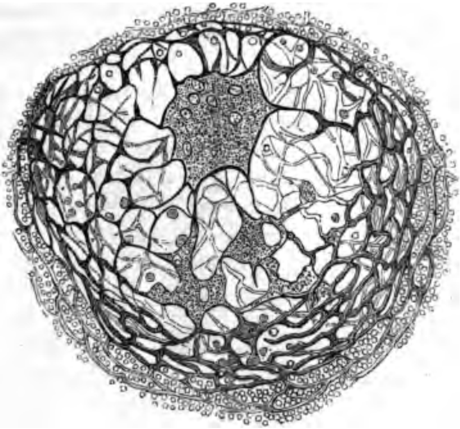
FIG. 50.



A Multinucleated Cell from the Lung in a case of Chronic Phthisis. Showing the large number of nuclei with bright nucleoli. × 400.

a bright nucleolus. (Fig. 50.) As many as forty nuclei may sometimes be counted in a single cell. Some of them are much smaller and contain only three or four nuclei. These smaller ones are much more regular in outline, and they probably represent an earlier stage of development than the larger cells. Four or five of these nucleated masses are sometimes found in a single tuberculous nodule, and they appear most commonly to occupy the centres, already alluded to, around which the lymph-like elements are grouped. (See Fig. 55.) The branched processes, which are continuous with the tuberculous reticulum, sometimes form wide meshes in the immediate vicinity of the multinucleated cell. These meshes are, according to Dr. Schüppel, filled with epithelial-like elements. These

FIG. 51.



A Multinucleated Cell from a Grey Miliary Tubercle of the Lung in a case of Acute Tuberculosis. Showing the wide empty meshes in the immediate vicinity of the cell. The branched processes are *directly continuous* with the reticulum of the tubercle. *× 200.*

last named elements the author has failed to observe, and when the meshes exist he has usually found them empty. (Fig. 51.) In some cases the author observed smaller nucleated nodules continuous with the processes of the larger cell; this appearing to indicate that new cells were originating from the protoplasmic prolongations. (See Figs. 49, 51.)

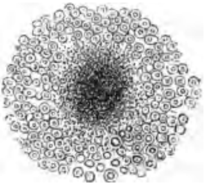
Although the above characters are to be observed in the multinucleated cells in successful preparations and in certain stages of the tuberculous growth, many of them will usually be found wanting. The nuclei and processes will only occasionally be seen, and the large cell commonly appears as a yellowish somewhat granular mass in which neither nuclei nor processes are visible. This is probably owing to the early retrogressive changes which these bodies appear to undergo. In this imperfect state, the author has observed these large cells in tuberculous nodules from most of the organs in which tubercle is met with.

Respecting the pathological significance of these multinucleated cells—they appear to the author to be merely characteristic of chronic inflammatory processes in lymphatic structures, whether these be limited to small circumscribed areas, as in tuberculosis; or whether they involve wider tracts of tissue, as in many forms of chronic induration. He has found them in portions of the indurated fibroid lung of chronic phthisis, in which there was neither caseation nor any indication of a nodular lesion. In the researches of Dr. Schüppel, already alluded to, they were met with in the most typical form in tubercular processes in lymphatic glands. They appear, further, to be more fully developed in the more chronic forms of tuberculosis, whilst in those cases in which the nodules are very rapidly produced, they are much smaller and less readily discernible. With regard to the histological elements from which they originate, nothing can certainly be stated. It would appear probable, however, that they spring either from the endothelium of the lymphatics or from the cells of the connective tissue; elements, it must be remembered, which are analogous to one another in their physiological functions. Looking at their anatomical relation with the other portions of the tuberculous nodules, they would seem to be especially concerned in the production of the fibrillated reticulum.

Although the structure which has been described is that of the most common form of lesion in acute tuberculosis—the *grey granulation* or *miliary tubercle*, it must be borne in mind that all the lesions are not thus constituted. When treating of the changes in the several organs, it will be seen that the precise anatomical constitution of the nodules varies somewhat, according to the characters of the tissue in which they originate. In the lung, for example, many of them consist largely of accumulations of epithelial-like cells within the pulmonary alveoli.

The lesions which may thus vary in their anatomical characters, vary also in the changes which they may subsequently undergo. The larger and more diffuse lesions usually undergo retrogressive fatty changes—they soften and become yellow and caseous. The minute lesions, on the other hand—those which are known as grey miliary tubercles—may either degenerate or become developed into a more or less completely fibrillated structure. In the former case, the grey translucent nodule becomes opaque and slightly yellow in its centre, and softens in consistence (Fig. 52); *in the latter—the* delicate intercellular material gradually *becomes developed* into a densely fibrillated network,

FIG. 52.



One of the Grey Nodules from the Lung in a case of Acute Tuberculosis, which is becoming opaque and soft in the centre. (Diagrammatic.)

the cells at the same time diminish in number, and the nodule becomes firmer, almost cartilaginous, in consistence. Which of these changes takes place appears partly to depend upon the severity of the infective process. The more intense the irritation, the greater is the tendency to the degeneration and softening of the nodules, the less intense and more chronic the process, the more liable are the miliary lesions to become fibrous.

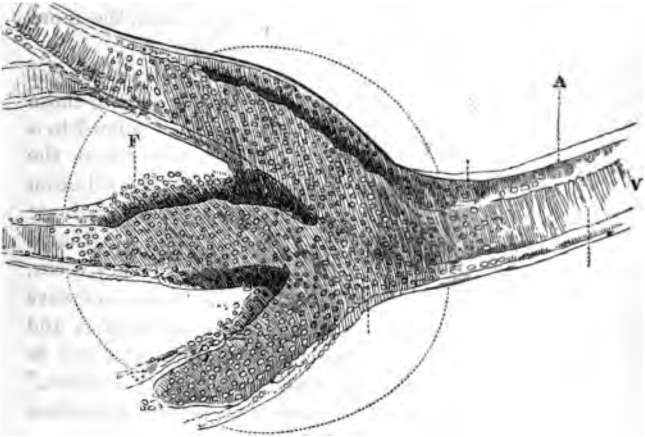
Before concluding the consideration of the general pathology of tuberculosis, allusion must be made to those cases in which the tuberculous processes are confined to a single organ. This limited tuberculosis differs from the more general one only in the extent of the distribution of the infective materials. The miliary lesions originate from some retrograde inflammatory product situated usually in the same organ as that in which they occur, and their limitation is probably owing to the infective substances being disseminated by the lymphatics and serous canals and not by the blood-vessels. This will be again referred to in the chapter on "Pulmonary Phthisis," and also in the following description of the tuberculous process as it occurs in the several organs and tissues.

TUBERCULOSIS OF THE PIA MATER.

In the pia mater the tuberculous process is associated with inflammation of the meninges, constituting the condition known as *tubercular meningitis*. This is almost invariably a part of a general tuberculosis.

The process is almost exclusively confined to the pia mater at the base of the brain, and is usually most marked in the Sylvian fissures. A few scattered granulations are, however, frequently visible on the upper surface of the hemispheres. The inflammatory growth originates in the perivascular lymphatic sheaths which enclose the small arteries of the pia mater. (Fig. 53.) The cells of the sheath multiply, and the process of proliferation commencing at separate centres, numerous small grey nodules are produced around the vessel. These, which are distinctly visible to the naked eye, cause an external bulging of the sheath, and a diminution in the calibre, or even complete obliteration, of the enclosed vessel.

FIG. 53.



Miliary Tubercle in the Pia Mater. The dotted line indicates the original size of the tubercular nodule. A. The lymphatic sheath. V. The bloodvessel. F. Proliferation of elements within the sheath. × 100. (Cornil and Ranvier.)

The localized obstructions to the circulation which result from the pressure of the perivascular nodules cause intense hyperæmia of the collateral vessels, and thus the pia mater at the base of the brain becomes exceedingly vascular, there being in some cases rupture of the vessels and extravasation. This is followed by a more general inflammatory process—a true basic meningitis. A transudation of the liquor sanguinis takes place from the hyperæmic and injured vessels, blood-corpuscles escape, and thus the meshes of the pia mater become infiltrated with a sero-fibrinous liquid, which in many parts has a puriform character.

These changes in the pia mater at the base of the brain are attended by softening of the immediately subjacent cerebral substance, which becomes infiltrated with young cells. The lateral ventricles at the same time become distended with serosity (acute hydrocephalus), so that the convolutions on the surface of the hemispheres are seen to be much flattened. The ependyma and choroid plexus also become exceedingly vascular, and the walls of the ventricles, together with the fornix and soft commissure become much softened. All of these changes are owing, partly to an inflammatory process, and partly to the mechanical obstruction to the circulation caused by the tuberculous growth. In addition, the arachnoid membrane is dry and sticky.

TUBERCULOSIS OF LYMPHATIC GLANDS.

In the lymphatic glands, the tuberculous process gives rise in the first place to inflammatory changes in the peripheral portions of the gland, inasmuch as it is with these that the infective materials which are conveyed by the lymphatic vessels first come into contact. The cellular elements increase in size, their nuclei multiply, and new elements are formed. As the process extends the gland becomes enlarged, the distinction between its medullary and cortical portions becomes lost, and it becomes changed to a greyish homogeneous mass. The new growth rapidly becomes caseous, the degeneration usually commencing at several separate centres; and when caseous the gland may subsequently soften, dry up, or calcify.

TUBERCULOSIS OF MUCOUS MEMBRANES.

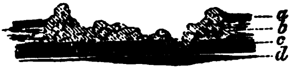
In mucous membranes the development of tuberculous nodules is usually secondary to some primary inflammatory process which leads to ulceration of the membrane. The intestinal, the urino-genital, and the respiratory mucous membranes may all be the seats of a tuberculous growth, but it is in the former that it constitutes the most frequent and most important change.

The Intestine.—In the intestine the occurrence of true tuberculous processes appears to be almost invariably preceded by primary inflammatory changes in the intestinal lymphatic structures. These changes have their seat in the solitary and Peyer's glands, and as in typhoid fever, it is especially these structures in the lower part of the small intestine and in the cæcum which are affected.

The first stage of the process consists in an inflammatory hyperplasia of the lymphatic elements. The solitary glands and patches thus become increased in size, and project with undue prominence above the surface of the membrane. The newly formed elements then undergo retrogressive changes—they soften and caseate, the degeneration in the patches commencing at several separate centres, and often extending until the whole patch becomes destroyed. As the result of these primary inflammatory changes an irregular ulcerated surface is produced, the floor and edges of which are more or less thickened owing to the extension of the inflammatory process into the submucous connective tissue. This is a simple ulcer, and its production, so far, is quite independent of a tuberculous process.

What must be regarded as a tuberculous change occurs subsequently to the primary ulceration, and it results in the development of small nodules of induration in the floor of the primary ulcer. The development of these nodules appears to take place principally around the blood-vessels, and as these are arranged transversely around the intestine, the new growth proceeds in the same direction. These secondary nodules of induration, like the primary inflammatory product, soften and become caseous, and thus the process of ulceration gradually *extends transversely* until the whole circumference of the gut may be destroyed. The ulcer thus produced presents a strong contrast to that of typhoid. Its edges and base are thickened and indurated, and the nodules of new growth, tending to become caseous, are seen scattered in its floor. (Fig. 54.)

FIG. 54.



A Tubercular Ulcer of the Intestine. (Diagrammatic.)
a. Epithelial lining. *b.* Submucous tissue.
c. Muscular coat. *d.* Peritoneum.

The tubercular ulcer rarely, if ever, heals, owing to the thickening of the tissues at its base. Perforation is quite an exceptional occurrence. In the process of its extension the ulceration is attended by some contraction and narrowing of the gut.

TUBERCULOSIS OF THE LUNGS.

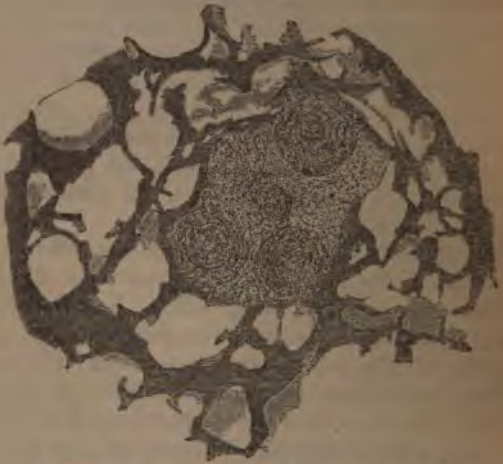
Tuberculous processes occur in the lungs as a part of a general tuberculosis, and also in many cases of pulmonary phthisis. The nature of the resulting inflammatory lesions is similar in both. It will be well, however, in the present place, more particularly to describe these lesions as they occur in the general infective disease. The more limited processes which take place in many cases of phthisis will be again referred to in a subsequent chapter devoted to the consideration of this affection. (See "Pulmonary Phthisis.")

The pulmonary lesions met with in general tuberculosis consist, for the most part, of disseminated nodular growths, which are universally known as "miliary tubercles." These growths are of two kinds—the *grey* and the *yellow*. The grey are semi-transparent nodules of a greyish-white colour, varying in size from a small pin's head to a hempseed. They are somewhat spherical in shape, and usually possess a well-defined outline. Sometimes they are firm, and almost cartilaginous in consistence; whilst in other cases they are much softer, and almost gelatinous. These softer forms, instead of being semi-transparent, are opaque and white. The yellow are, for the most part, larger than the preceding, many of them much so, some being as large as a pea. They are also softer in consistence, less defined and regular in outline, and they pass more insensibly into the surrounding tissue. Many of them possess a greyish-white translucent margin, which may be pretty firm in consistence, but never so hard as are many of the grey nodules, whilst their central portions are opaque, yellowish, or caseous. These nodules, both the grey and the yellow, although generally scattered, are sometimes confluent in groups.

Both the grey and the yellow nodules are often found associated in the same lung; in other cases the grey nodules only are met with, whilst, less frequently, nearly all the growths are of the yellow variety. The condition of the pulmonary tissue which is situated between the nodules, varies considerably. It may be perfectly normal, more or less congested and œdematous, or it may present varying sized tracts of greyish, granular, friable consolidation. A perfectly normal condition of the intervening pulmonary tissue is found in many of those cases, in which all the growths are of the grey variety; but when there are numerous yellow nodules, the lungs are nearly always more or less congested or consolidated.

When these nodules are examined microscopically they are seen to exhibit two different kinds of structure—viz., the small-celled lymphoid tissue, which has been already described as that which is the most characteristic of *tuberculous lesions,* and accumulations of large nucleated cells within the pulmonary alveoli (catarrhal pneumonia). There is, however, this marked anatomical difference between the various kinds of nodules—that whereas most of the smaller grey ones are constituted entirely of the first-named tissue, the larger grey, and most of the yellow ones, consist largely of the alveolar accumulations. When the small grey nodules are examined with a low magnifying power, they usually appear as little, somewhat spheroidal, masses situated between the alveoli, the latter presenting a perfectly normal appearance. (Fig. 55.) When more highly magnified, they are seen to consist of the characteristic tubercular structure—viz., small *lymph*-like corpuscles grouped within the meshes of a *fibrillated* network (see Fig. 48); associated with which

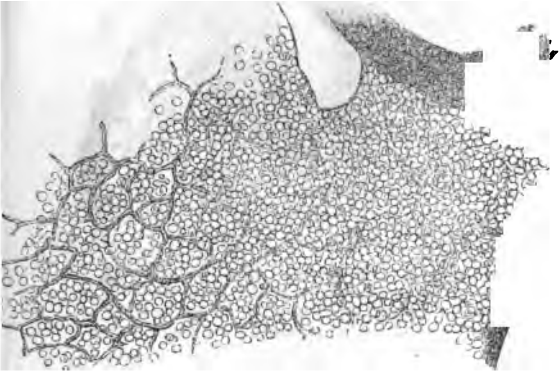
FIG. 55.



A firm Grey Tubercle from the Lung in a case of Acute Tuberculosis. Showing the situation of the tubercle *between* the alveoli, the latter presenting a perfectly normal appearance. The grouping of the elements around separate centres is also seen. × 33.

may be two or three of the large multinucleated cells. The central portions of some of them consist simply of minute granules, the elements having evidently undergone retrogressive changes. They are intimately incorporated with the pulmonary tissue; the walls of many of the alveoli, which are immediately adjacent to the nodule, being thickened by a new nucleated tissue precisely similar to that of the nodule itself. (Fig. 56 *a.*) The conformation of some of these nodules is not quite so simple, but as the new growth extends by a progressive implication of the alveolar walls, it encroaches upon, and gradually obliterates the immediately adjacent alveolar cavities.

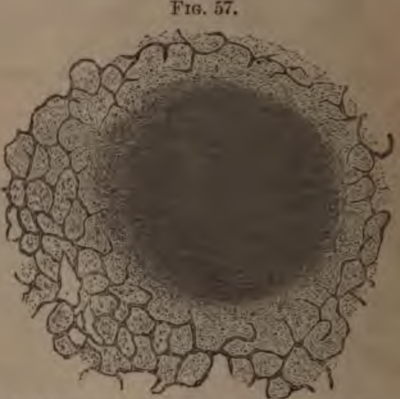
FIG. 56.



A small portion of the most external part of a firm Grey Tubercle from the Lung in a case of Acute Tuberculosis. Showing the structure of the nodule; and at *a* its incorporation with the alveolar wall. × 270.

The constitution of the larger grey, and of most of the yellow nodules, differs somewhat from that of the smaller grey ones above described. When these are examined with a low magnifying power, it is seen that they are not like most of the smaller grey nodules, simply inter-alveolar growths, involving merely the alveolar walls, but that their more external portions are made up of *accumulations within the alveolar cavities.* (Fig. 57.) When somewhat more highly magnified, their

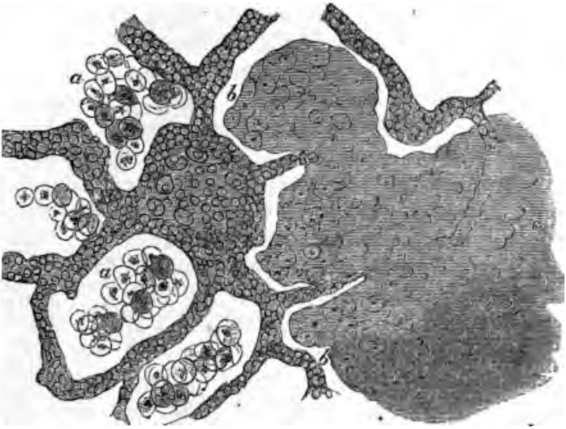
FIG. 57.



A Yellow Tubercle from the Lung in a case of Acute Tuberculosis. Showing the accumulations within the alveoli at the peripheral portions of the nodule, and the degeneration in the centre. × 33.

constitution at once becomes apparent. (Fig. 58.) Their central portions (*c*) consist, for the most part, of a structureless granular débris, in which, perhaps, here and there, traces of formed elements are visible. More externally, are seen indications of alveoli, which are filled with partially degenerated epithelial-like cells (*b*), with, in some parts, small tracts of a small-celled tissue resembling that met with in the grey nodules; whilst in the peripheral portions of the growth (*a*) the alveolar cavities are quite distinct, their walls are infiltrated with a small-celled growth, and their cavities are filled with large nucleated cell-forms similar to those which are lways to be found in the alveolar cavities of the healthy ng. In short, it is clear that the structure of most of ese nodules more closely resembles a lobular catarrhal

FIG. 58.



A small portion of the most external part of a Yellow Tubercle from the Lung in a case of Acute Tuberculosis. Most externally at *a* are seen the alveoli filled with epithelial-like cells. More internally at *b* both the alveolar walls and the epithelial contents are seen in the process of degeneration; whilst in the central portions, *c*, the degeneration is so far advanced that all trace of structure is lost. The alveolar walls are thickened by a small-celled growth, and at one part a minute mass of this small-celled tissue is visible. × 140.

neumonia than that met with in the smaller grey rowths; and that although the walls of the alveoli are hickened by a small-celled tissue similar to that which onstitutes the latter growths, and small tracts of the ame tissue may be found in the central portions of the odule, the nodule consists, in the main, of alveoli stuffed with epithelial-like cells, which have a *special* tendency to ndergo rapid retrogressive changes.

Respecting the cause of these differences in the anatomical constitution of the miliary lesions in the lungs—the author believes that they depend upon differences in the intensity of the inflammatory processes. The more severe the irritation of the infective particles, the more liable are these to cause a proliferation of the large epithelial-like cells contained within the alveoli; whereas when the irritant is less severe, its influence tends to be limited to the elements immediately adjacent to the blood-vessels and lymphatics, and the development of a small-celled tissue is consequently the result. (See "Chronic Inflammations.") Further—the large epithelial-like cells, being probably incapable of further development, quickly degenerate; whilst the small-celled tissue, although it may undergo similar retrogressive changes, very frequently becomes developed into a more or less completely fibrillated structure.*

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* In explaining the peculiar *lymphoid* characters of the new growth which is developed both in the alveolar walls and in the interlobular tissue as the result of chronic inflammatory processes in the lungs, it is important to bear in mind the more recent additions to pulmonary histology. Not only does this lymphoid tissue exist largely in the neighbourhood of the smallest bronchioles, but the alveolar walls are richly supplied with lymphatics, and the recent investigations of Buhl and others seem to show that the large nucleated cells which line the alveoli are not epithelial, but correspond with lymphatic endothelium.

CHAPTER XXVI.

PYÆMIA AND SEPTICÆMIA.

It is proposed, in the present chapter, very briefly to describe some of the more important phenomena which result from infection by means of the products of certain *acute* inflammatory processes. These phenomena include what are known as *traumatic* or *inflammatory fever*, *septicæmia*, and *pyœmia.*

When a person receives an external injury sufficient to cause an inflammatory process of considerable extent and intensity in the part injured, this process is usually followed by a general disorder of the vital functions, the most prominent symptom of which is pyrexia. This pyrexia, which so commonly occurs after surgical operations and other extensive local injuries, is what is usually known as *traumatic* or *inflammatory fever.* Respecting the cause of this pyrexia—it is due to the absorption of some of the products of the local inflammatory process, and possibly also in some cases, to that of substances resulting from the decomposition of dead organic matter in the neighbourhood of the injury. In other words, the pyrexia and other phenomena result from the dissemination of certain infective materials from a focus of acute inflammation.

Between this traumatic or inflammatory fever and what is known as septicæmia there is no line of demarcation—*the one passes* imperceptibly into the other.

When the general disturbance of the vital functions is considerable, and gives rise not only to pyrexia, but also to a tendency to vomiting and diarrhœa, and ultimately to a condition of coma and collapse which tends to terminate in death, the state is termed one of *septicæmia.* Septicæmia appears therefore to differ from simple traumatic fever mainly in this—that in it the general infective process is one of much greater intensity. In both there is usually an absence of any characteristic local lesions. After death the blood may be found to be somewhat darker and less firmly coagulated than natural; the spleen and liver enlarged and abnormally vascular; and, if there has been diarrhœa, the intestinal mucous membrane may present the appearance of acute catarrhal inflammation with some swelling of the lymphatic structures. In some cases also there is pleurisy or pericarditis.

The general infective process known as *pyæmia* differs from both traumatic fever and septicæmia in this respect—that in it the dissemination of the infective substances derived from the inflammatory focus gives rise not only to that general disturbance of the vital functions which characterizes these two conditions, but also to the formation of metastatic nodules of induration which soon assume the character of abscesses, and to more diffused inflammatory lesions. These metastatic nodules of induration which so quickly become purulent, and are so characteristic of the disease, present certain peculiarities. In their earlier stages they usually consist of somewhat reddish, friable, granular-looking masses of consolidation, which are surrounded by a thin zone of red hyperæmic tissue. These masses are frequently wedge-shaped, the apex of the cone being towards the centre of the organ. They vary considerably in size, some not being larger than a small pea, whilst others exceed the size of a chestnut. The consolidated mass soon assumes the characters of an abscess. Its more central portions become softened and purulent, and ultimately it tends to become converted into a collection of pus and broken-down tissue, this being still surrounded by a thin red zone of induration.

These metastatic abscesses are met with most frequently in the lungs; but they also occur in the liver, spleen, kidneys, and in other internal organs. They are more commonly found near the surface than in the more internal portions of the organ, often being situated immediately beneath the fibrous capsule.

The more diffused inflammatory processes which also occur in pyæmia, consist chiefly in suppurative arthritis and inflammation of the serous membranes, especially of the pleuræ and pericardium.

Although the occurrence of metastatic abscesses in the later stages of many of these acute infective processes has served as a basis for their classification—those in which they occur being termed pyæmic, those in which they are absent, septicæmic—it is probable that it does not justify the conclusion that there exists between them any essential pathological difference. Both pyæmia and septicæmia result from the absorption of certain infective substances from some focus of acute inflammation. The effect of these substances may be simply to produce a general disturbance of the vital functions—a septicæmia; or, more remotely, to cause various disseminated suppurative inflammations—a pyæmia; and as in other acute infective diseases—*e.g.*, scarlet fever, death may result from the general disturbance of function quite independently of any local lesions, so in the diseases now under consideration a septicæmia may be the cause of dissolution without the occurrence of any of those metastatic products which are regarded as characteristic of pyæmia. Such being the case, it is evident that whereas a septicæmia may exist without the subsequent development of *metastatic lesions—a* pyæmia, pyæmia must always be associated with more or less septicæmia. In other words, pyæmia is a septicæmia in which there are metastatic suppurative inflammations.

Having thus pointed out the close pathological relation which subsists between these acute infective processes, it remains to consider somewhat more fully the nature of the infective substances, and to explain the occurrence of the metastatic lesions.

The infective substances, as already stated, originate in the products of certain acute inflammatory processes. Further—the inflammatory processes which constitute the infective foci are in the great majority of cases the direct results of some *external* injury, an injury producing a lesion which communicates with the external air. These external inflammations resulting from injury usually only give rise to that comparatively slight disturbance of the vital functions which is known as traumatic or inflammatory fever, and this disturbance appears to be owing to the absorption of the *unaltered products of a healthy inflammatory process.* When the local inflammation gives rise to a septicæmia or pyæmia, this result is with equal probability due to the absorption of *inflammatory products which are altered by the presence of certain abnormal subtances.*

With regard to the nature of the abnormal substances which give to the inflammatory products their septic characters, we are at present unable to speak with absolute certainty. It must, however, be regarded as in the highest degree probable that these substances usually result from the putrid decomposition of the pus and inflammatory liquids produced by the local inflammation. Much light has been thrown upon this subject by comparative pathological research. Dr. Burdon-Sanderson, in a series of observations made in the laboratory of the Brown Institution to determine the nature of the pyæmic poison, finds that in pyæmia and septicæmia as produced in the lower animals, *bacteria* abound in all the inflammatory liquids; and also that these same organisms exist in the blood.* He finds further, that these pyæmic inflammatory liquids, when introduced into the circulation or into one of the serous cavities of another animal, produce the symptoms of pyæmia, and that the intensity of these symptoms appears to bear some direct proportion to the number of bacteria which the infective liquids contain. Those animals which were inoculated with liquids containing very numerous bacteria and of intense infective power, died rapidly with symptoms of septicæmia; whereas in those in which the inoculated liquids contained fewer bacteria and were less active, the process was more protracted and was attended by the development of metastatic abscesses—a pyæmia. The results of these investigations therefore show that, in the lower animals, bacteria are invariably present in liquids which are capable of inducing pyæmic processes, and it must be admitted as exceedingly probable that in the disease as it occurs in man, the presence of these or similar organisms in the inflammatory products is in some way intimately connected with their infective characters.

The probability of the generation of the pyæmic poison being intimately associated with the presence of minute organisms in the inflammatory products is increased by the fact, that the disease is in the very great majority of cases secondary to inflammatory lesions which communicate with the external air—a condition the most favourable to the entrance of these organisms from without. It must, however, be borne in mind that pyæmic processes occasionally occur under circumstances in which no external point of inflammation is discoverable. In explanation of these very exceptional cases the results of Dr. Sanderson's experiments, already alluded to, are of much value.

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* "*Trans.* Path. Soc. Lond.," 1872.

Dr. Sanderson finds that pyæmia may be induced in the lower animals by the introduction into one of their serous cavities of liquids produced by an inflammatory process which has been set up by chemical agents under circumstances which preclude the possibility of the introduction of any infecting substances from without—liquids, however, which, like those derived from an external inflammatory lesion, abound in bacteria.

The remaining point for consideration is the pathology of the disseminated secondary inflammations—the diffuse lesions and the metastatic abscesses. The most common diffuse inflammatory lesions which result from the pyæmic process are suppurative arthritis, inflammation of the serous membranes, and of the subcutaneous cellular tissue. The mode of origin of these diffused inflammatory processes we are unable certainly to explain. They probably occupy the same pathological position as the diffuse inflammations which occur in other infective diseases—*e.g.*, in scarlet fever and acute tuberculosis.

Our knowledge of the pathology of the metastatic abscesses is much more complete. These appear usually to be of *embolic origin*, the emboli originating in the venous thrombi which form at the focus of primary inflammation. The circumstances under which thrombi formed in the vessels of a part become softened or broken-up so as to furnish embolic plugs, and the way in which these plugs may set up acute inflammatory processes at the seat of their arrest, will be fully described in the chapters on "Thrombosis" and "Embolism."* It will be sufficient in the present place to state that in the course of a pyæmic process the coagula which form in the vessels at the seat of the primary inflammation become infected with the pyæmic poison; and if they soften or become ken-up so as to furnish embolic plugs, these plugs se secondary suppurative processes in the parts in ch they become arrested; and it is to the dissemi- ion of these infective emboli that the formation of majority of the metastatic abscesses in pyæmia is ng.

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* The student will do well to read the chapters on "*Thrombosis*" and "Embolism" as a sequel to the present chapter.

CHAPTER XXVII.

SYPHILIS.

THE lesions occurring in the course of constitutional syphilis are for the most part inflammatory in their nature, but in their seat, distribution, and anatomical characters, some of them present certain peculiarities which make them quite characteristic of this disease. The primary syphilitic lesion (usually the indurated chancre), the secondary lymphatic gland enlargement, and the subsequent series of changes in the skin, mucous membranes, and later—in the nervous system, bones, and internal organs, are all of them the results of chronic inflammatory processes induced by the syphilitic poison.

The lesions, however, which must be regarded as especially characteristic of constitutional syphilis are of two kinds—certain fibroid indurations, and a form of nodular growth which is known as a *gumma* or syphilitic tumour. These two forms of lesions are frequently associated, and in many cases it becomes difficult to draw a sharp line of demarcation between them. A growth which in its earlier stages is simply connective tissue, may subsequently assume, either in whole or in part, the characters of a gummy tumour.

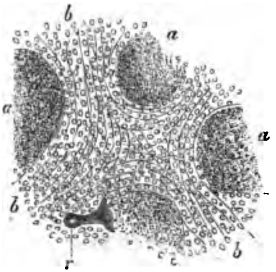
The fibroid changes usually occur somewhat earlier in the course of constitutional syphilis than the gummy growths. The new tissue consists in the first place of an embryonic small-celled structure, which subsequently becomes more or less completely fibrillated (see "Inflammation of Common Connective Tissue"). The fibroid thickenings which result are characterized by the great irregularity in their distribution. They occupy, for the most part, small areas; or, if more extended, they are much denser in some parts than in others. It is these peculiarities in their distribution and localization and not their anatomical characters which render them so characteristic of syphilis.

These fibroid changes are met with in various situations—in the periosteum, in the sheaths of nerve-trunks, in the capsule and interstitial tissue of organs, and in muscle. When occurring in the capsules of organs they present very characteristic appearances. In the liver and spleen, where they are the most frequent, they give rise to an irregularly distributed thickening and puckering of the capsule which is exceedingly typical of advanced syphilis. The thickened portions are often connected with dense fibrous septa which pass into the interior of the organ; and there are usually also numerous strong peritoneal adhesions.

Fibroid changes occurring in the interstitial tissue of organs are most common in the liver, and here they are almost invariably associated with the thickening of the capsule which has been alluded to. The change in the liver sometimes resembles somewhat that which occurs in ordinary cirrhosis. It usually, however, differs markedly from cirrhosis in this respect—that the growth of new tissue is much less regular and uniform, occurring only in certain regions or around certain branches of the portal vein. Frequently the new tissue originates from only two or three centres, and thus a corresponding number of dense fibroid cicatrices are produced in the organ. Owing to this localization in the development of the cicatricial tissue the liver becomes much more irregularly puckered and contracted than in cirrhosis, and the obstruction to the portal circulation is almost *nil*. Gummy growths frequently originate in the fibrous septa. In other cases the interstitial change is much more general, more resembling that of ordinary cirrhosis. This is especially the case in congenital syphilis.

The other variety of lesion, which is perhaps more characteristic of syphilis than the preceding, is the *gumma* or syphilitic tumour. The gummata were formerly regarded as non-inflammatory neoplasms, and were classified by Virchow amongst what he termed the "granulation" tumours. As usually met with, they are moderately firm yellowish-white nodules, having often, on section, somewhat the appearance of a horse-chestnut. They vary in size from a hemp-seed to a walnut, and are surrounded by a zone of translucent fibrous-looking tissue, which sometimes has the appearance of a capsule, and which is so intimately associated with the surrounding structures that the complete enucleation of the mass is impossible. In the earlier stages of their development, when they less commonly come under observation, they are much softer in consistence, more vascular, and of a reddish-white colour; whilst in their most advanced stages, owing to extensive retrogressive changes, they may be distinctly caseous.

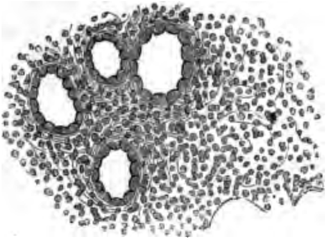
FIG. 59.



Gummy Growth from Liver. a. Central portions of growth, consisting of granular débris. *b.* Peripheral granulation tissue. *r.* A blood-vessel. × 100. (Cornil and Ranvier.)

When the gummata are examined microscopically they are found to consist in the main of atrophied, degenerated, and broken-down cell-products, embedded in an incompletely fibrillated tissue. There are, however, some marked structural differences between the central and external portions of the growth. The central portions are composed almost entirely of closely-packed granular débris, fat granules, and cholesterin, amongst which may be an exceedingly scanty fibrillated tissue. (Fig. 59, *a.*) Surrounding this and directly continuous with it is a more completely fibrillated structure; whilst the peripheral portions of the growth, which are continuous with the surrounding tissue, consist entirely of small round cells—the granulation or "indifferent" cells. (Fig. 59, *b*, and Fig. 60.) The blood-vessels, which only exist in the external portions of the growth, are very few in number.

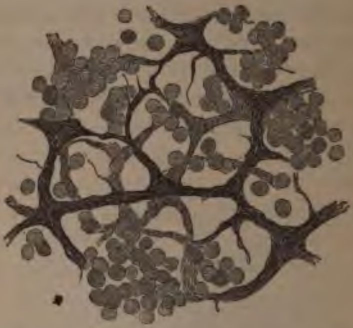
FIG. 60.



The Peripheral Portion of a Gummy Growth in the Kidney. Showing the small-celled growth in the intertubular tissue. × 200.

The three zones above described, which are to be distinguished more or less clearly in most of the gummy nodules, correspond with three different stages in their growth. The most external zone, consisting of the granulation-tissue, represents the earliest stage of development, and by the continuous formation of this tissue the growth may continuously increase. The intermediate fibrous zone represents the second stage in the process—the development of the granulation tissue into a more or less completely fibrillated structure. The characters of this fibrillated tissue vary in different growths. In some the fibrillation is very distinct; in others, the tissue is dense and cicatricial in character; whilst less frequently, it consists of a reticulated structure within the meshes of which are grouped small round cells. (Fig. 61.) This somewhat resembles the follicular structure of a lymphatic gland (compare with Fig. 63, A). The central zone, consisting of the amorphous granular material, represents the oldest portion of the growth—that which has undergone retrogressive changes. The blood-vessels, which only exist in the zone of proliferation, appear to become obliterated in the process of development; and this probably accounts for the rapid degeneration of the central portions of the growth. When the tumour is large, it may sometimes be seen to be made up of several distinct smaller growths, each presenting at its circumference the more perfect cells, whilst its central parts are granular and amorphous.

FIG. 61.



From a Gummy Growth in the Kidney. Showing the adenoid structure occasionally met with in the intermediate zone of these formations. × 200.

It would thus appear that the first stage in the process of formation of these gummy growths consists in the production of a granulation tissue. This is followed by the incomplete development of the new tissue into a fibrillated structure, together with the atrophy and degeneration of the young elements. The degenerated elements become closely packed in the centre of the growth, whilst proliferation and incomplete fibrillation continue at the circumference.

The gummata are the new formations most characteristic of syphilis, and their distribution is almost coextensive with that of syphilitic lesions. They are met with in the skin and subcutaneous cellular tissue, in the submucous tissue, in muscle, bone, and in the connective tissue of organs—especially of the liver, brain, testicle, and kidney. When situated in the submucous tissue the mucous membrane may become destroyed, and a deep ulcer form. This is seen in the pharynx, soft palate, tongue, larynx, and in other parts. These true gummy ulcerations must be distinguished from the superficial ulcerations resulting from inflammatory processes in the lymphatic structures, which also occur in syphilis.

CHAPTER XXVIII.

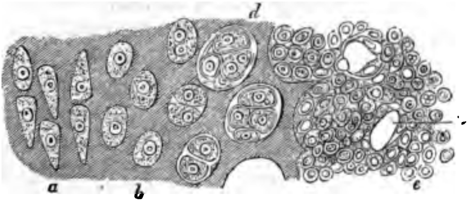
INFLAMMATION OF NON-VASCULAR TISSUES.

INFLAMMATION OF CARTILAGE.

THE phenomena of inflammation in cartilage have been principally studied by the artificial irritation of the articular cartilages in the lower animals. They consist in changes in the cartilage itself, and in the vessels of the adjacent synovial membrane and bone, from which the cartilage receives its nutritive supply. Respecting the vascular changes, these are such as have been already described as characteristic of inflammation.

In the cartilage itself, the cells enlarge within their capsules, their nuclei become more prominent and their protoplasm more granular. The cells then divide and multiply, so that each cavity contains numerous young cells which ultimately closely resemble pus-corpuscles. At the same time the capsules are destroyed, and the intercellular substance softens and breaks down into a finely granular material. (Fig. 62.) As the intercellular substance becomes destroyed, the newly-formed cells and granular débris escape from the surface of the cartilage, which thus becomes irregular, presenting numerous elevations and depressions: this is ulceration of cartilage. Whilst these changes are taking place in the cartilage itself, numerous new vessels are produced. These extend over the surface of the inflamed cartilage and penetrate its substance. This process of softening and ulceration may go on until the cartilage is completely destroyed; but it may become arrested. In the latter case the newly-formed cells form a granulation-tissue which subsequently fibrillates, and the lost cartilage thus becomes replaced by a fibrillated tissue.

FIG. 62.



Section of Inflamed Cartilage. *a.* The normal cartilage-cells. *b.* The same enlarged. *d.* Multiplication of cells within their capsules. *e.* Great increase in the number of the young cells, and destruction of the intercellular substance. × 250. (Cornil and Ranvier.)

When the inflammation is less severe and runs a more chronic course, the cell-proliferation is not so active, and the intercellular substance is less destroyed. The newly-formed cells are more highly organized, and whilst many of them form a fibrillated tissue others undergo retrogressive changes. Irregular cavities may thus be produced in the midst of a fibrillated cartilage.

INFLAMMATION OF THE CORNEA.

The process of inflammation as it occurs in the cornea has been chiefly studied in the frog. After irritation of the frog's cornea, the earliest changes observed consist in the conjunctival epithelium becoming visible, and the appearance amongst the epithelial cells of a few leucocytes, which have probably escaped from the hyperæmic vessels of the conjunctiva. The cornea-corpuscles and their prolongations then become visible (they are invisible in the healthy cornea, which appears perfectly structureless), and the prolongations are the seat of slight amœboid movements. At a somewhat more advanced stage the cornea-corpuscles become altered in form, their prolongations become much shorter, they lose their stellate outline, and gradually assume more the appearance of cartilage-cells. The next change observed in the enlarged and rounded corpuscles consists in their proliferation, and in the place of each corpuscle is seen a clump of young, round, amœboid cells, many of which are indistinguishable from the living corpuscles of pus.

Whilst these changes are taking place in the corpuscles of the inflamed cornea, the intercellular substance gradually becomes increasingly opaque, owing to its infiltration with young cellular elements (leucocytes). These are so numerous and increase so rapidly, that they must undoubtedly be regarded as in the main emigrant white blood-corpuscles; although from the changes observed to take place in the earlier stages of the process in the fixed elements of the cornea, it must be admitted that they are partly derived from the proliferation of the cornea-corpuscles. As the number of these young elements increases the consistence of the cornea becomes diminished, until ultimately the tissue breaks down and is destroyed.

The inflammatory process may continue until the whole of the substance of the cornea is softened and destroyed; or it may become arrested. In the latter case more or less thickening and opacity of the cornea will result, owing to the increase in the number of cells and the changes in the intercellular substance.

CHAPTER XXIX.

INFLAMMATION OF VASCULAR CONNECTIVE TISSUES.

INFLAMMATION OF COMMON CONNECTIVE TISSUE.

COMMON connective tissue is one of the most frequent seats of the inflammatory process, not only the subcutaneous connective tissue, but also the connective tissue of organs and of other parts.

If connective tissue be examined a few hours after the infliction of an injury, it will be found that in place of the fibrillated substance and fixed connective-tissue corpuscles of which it is normally composed, the tissue is infiltrated with amœboid cells (leucocytes), and that the fibrillated intercellular material has become homogeneous and gelatinous in consistence. The number of these cells gradually increases, and the intercellular substance gradually becomes more completely destroyed—being probably consumed by the newly-formed elements—so that ultimately the tissue consists almost entirely of small round cells held together by a very small quantity of soft gelatinous intercellular material.

Respecting the source from which these young elements are derived—*i.e.*, how far they are emigrants, and how far they are the offspring of cells belonging to the connective tissue—there appears to be little doubt that they are almost entirely emigrants. Although it was formerly supposed that the connective-tissue corpuscles multiplied very rapidly in inflammation, and that the newly-formed cells were entirely the result of their proliferation, the recent investigations of Professors Cohnheim and Stricker show that this view is erroneous; and according to Cohnheim, these corpuscles take no part whatever in the inflammatory process. Professor Stricker, however, has observed them undergoing active movements in the inflamed tongue of the frog, and although he has never seen them divide, he concludes that, like the elements of most other tissues, they probably do so in the later stages of the inflammatory process. The present state of our knowledge respecting inflammation of connective tissue would therefore appear to justify the conclusion that in the early stages of the process all the young cells are emigrants, but that most probably in the later stages many of them are derived from the proliferation of the connective-tissue corpuscles.

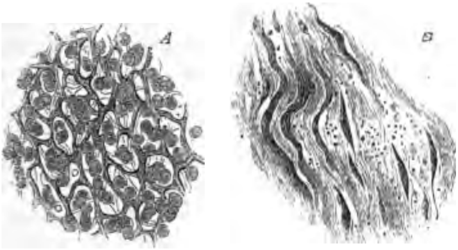
Such being the nature of the changes which more immediately follow injurious stimulation of the connective tissue—the inflammatory process may terminate in *resolution*, in *organization*, or in *suppuration*.

RESOLUTION.—If the injury sustained by the tissue is not severe, the inflammation may gradually subside, the process terminating in *resolution*. In this case the hyperæmia diminishes, the emigration ceases, some of the young cells undergo fatty metamorphosis and thus become absorbed, others pass into and are removed by the lymphatics, and the tissue gradually returns to its normal condition.

ORGANIZATION.—If the inflammatory process does not terminate in resolution, many of the young cells may become more fully developed and ultimately form a fibrillated tissue. This *organization* of the inflammatory formation is seen in the healing of wounds by the "first intention," and also in many of the interstitial inflammations of the kidney, liver, and other organs. In order for it to occur it is necessary that there should be a considerable diminution in the intensity of the inflammation. (See " Chronic Inflammations.")

The process of organization takes place by the production of new capillaries and by the development of the young cells into a granulation-tissue. This granulation-tissue consists almost entirely of young cells, which must be regarded as exhibiting a higher stage of development than the primary amœboid cells (leucocytes) of the inflammatory formation. They are spherical masses of protoplasm from $\frac{1}{1800}$ to $\frac{1}{3000}$ of an inch in diameter, usually containing an indistinct round or roundly-oval nucleus, which often only becomes visible after the addition of acetic acid; and although they exhibit slight amœboid movements, they are much less active than the emigrant blood-corpuscles. The further organization of the growth takes place by the development of this granulation-tissue into a fibrillated structure. Many of the granulation-cells gradually assume a spindle-shape, and probably in this way many of the fibres are produced. (Fig. 63, B.)

FIG. 63.



Varieties of Cicatricial Tissue. × 200.

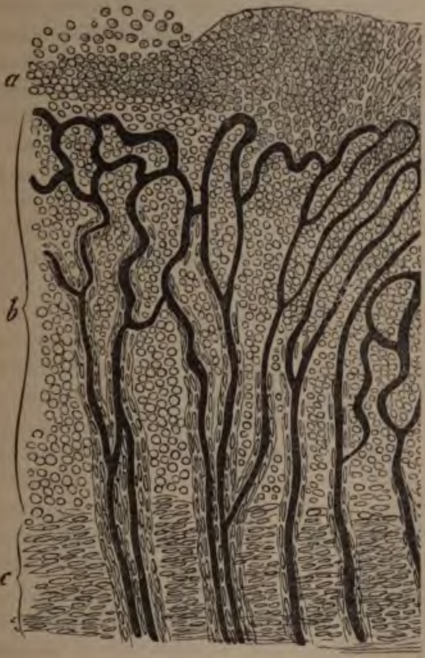
At the same time the fibrillation may be also due to a differentiation of the intercellular substance. The newly-formed capillaries gradually disappear, and the richly cellular tissue thus becomes converted into a more or less densely fibrillated structure, which is characterized by the gradual process of contraction which it undergoes. This is *cicatricial tissue.*

The characters of this cicatricial tissue present certain variations. Sometimes it consists of closely-packed wavy fibres, amongst which are a few elongated spindle-shaped elements, such as are represented in Fig. 63, B. It is equally common for the tissue to assume the appearance shown in Fig. 63, A—a dense homogeneous or obscurely fibrillated material, forming meshes of various sizes, within which are grouped a few spheroidal cells. (See also Figs. 48, 74.) These two varieties are very frequently associated in various degrees in the same specimen.

SUPPURATION.—When the injury sustained by the tissue is so severe or so prolonged in its action as to prevent the occurrence of resolution or of immediate organization, the young cells infiltrate the tissue in such numbers that they may accumulate so as to constitute pus. The pus may either become collected together within the tissue so as to form an abscess, or it may be continuously discharged from the surface, as in a granulating wound. The deleterious influence which the pus exercises upon the tissues with which it comes in contact, causing their destruction and absorption, has already been alluded to. (See "Suppuration.")

Organization after Suppuration.—This constitutes what is generally known as healing by *granulation*, or by the *second intention.* It takes place in wounds, in which, from the non-apposition of the wounded surfaces, union by the first intention has not been effected; and in other lesions in which the injured tissue presents a free surface communicating with the external air, as in an ulcer. The process of repair after the separation of a dead part (demarcation and separation) is in the same way effected by granulation, as is also the closing of the cavity left after the discharge of the contents of an abscess. In all these, and similar cases, the inflammation and suppuration of the tissue are followed by the formation of granulations, and by the subsequent development of these into a fibrillated structure.

FIG. 64.



A Granulating Surface. a. Layer of pus. b. Granulation-tissue with loops of blood-vessels. c. Commencing development of the granulation-tissue into a fibrillated structure. × 200. (Rindfleisch.)

The process of organization in these cases is effected in the first place by the development of the young cells in the superficial layers of the inflamed tissue into a granulation-tissue, in the same manner as when there is no suppuration. This granulation-tissue, however, being situated superficially, and coming into contact with the external air, becomes arranged in the form of small papilliform nodules, which are known as *granulations*. This arrangement of the granulation-tissue in the form of granulations, appears to be determined by that of the new capillary blood-vessels which are developed so rapidly in it. These vessels form little vascular loops, and the young cells are arranged round them, so that each loop corresponds with a single granulation. The deeper layers of the granulation-tissue gradually become developed into a fibrillated tissue, whilst the cells on the surface of the granulations, together with the liquids exuded from the subjacent vessels, are discharged in the form of pus. (Fig. 64.)

INFLAMMATION OF BONE.

Inflammatory processes in bone give rise for the most part to an increase of medullary tissue and to softening of the compact osseous structure.

The process takes place in the vascular medullary tissue. This becomes infiltrated with amœboid elements which have migrated from the hyperæmic vessels. The cells in the medullary spaces and Haversian canals enlarge and multiply; in those which contain fat—the adipose cells—the fat is first removed, and thus a tissue is formed similar to that met with in the medulla during the process of its development. This consists of numerous small round cells, larger cells containing several nuclei closely resembling the "myeloid cells," and a scanty soft intercellular substance. Whilst these changes are taking place in the medullary tissue, the surrounding osseous lamellæ are gradually absorbed, the lime salts are removed, and in this way the medullary spaces and Haversian canals increase in size and ultimately become confluent. There is thus a new formation of medullary tissue at the expense of the compact osseous structure, and the bone becomes exceedingly spongy, soft, and vascular.

As the process proceeds, and the cellular infiltration and formation of medullary tissue increase, the latter may ultimately make its way through the bone and appear as a fungating mass (granulations) beneath the periosteum or the articular cartilage. The extent of pus-formation will depend upon the severity of the inflammatory process. The pus may either accumulate within the cavities formed in the bone, or—as the osseous structure is absorbed and the medullary tissue becomes superficial—make its way to the surface.

The suppuration and rapid growth of tissue may be the cause of most deleterious ulterior changes in the bone. Owing to the interference with its vascular supply, which results from the pressure exercised by the pus and new tissue as it is confined within the unyielding osseous walls, or to the accumulation of pus beneath the periosteum, smaller or larger portions of the bone may lose their vitality (*Necrosis*), and the sequestra acting as foreign bodies keep up the inflammatory process. In other cases the death of the bone takes place only in minute portions, the process consisting rather in a molecular disintegration (*Caries*). As the inflammatory process ceases, or when from its commencement it is less severe, the newly-formed tissue may become developed into a compact osseous structure, which in some cases is much denser than the original bone (*Sclerosis*). Similar results are produced by inflammatory processes which are limited to the periosteum and to the immediately subjacent bone.

CHAPTER XXX.

INFLAMMATION OF BLOOD-VESSELS AND HEART.

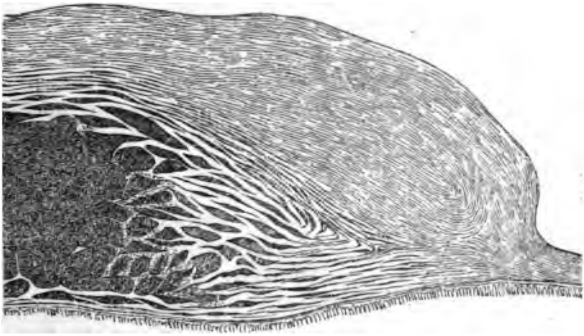
INFLAMMATION OF BLOOD-VESSELS.

INFLAMMATORY processes, both in the arteries and veins, are not unfrequently associated with the softening and breaking-down of coagula which have formed within the vessels, the softened coagulum being the *cause* and not the *result* of the inflammation. A description of these will be found in the chapter on "Thrombosis." Independently of thrombi, it is in the arteries that inflammatory changes are most frequently met with, where they give rise to the various alterations in the walls of the vessel which constitute what is usually known as *Atheroma.*

ATHEROMA.—The changes in the arteries known as atheromatous, have their seat in the deeper layers of the inner coat. In the earliest stage of the inflammatory process the fibrous and elastic lamellæ of the inner coat of the vessel become infiltrated with young cells, which are probably partly emigrants, and partly derived from the proliferation of the cells of these structures. As these young cells increase in number they give rise to a swelling beneath the innermost layers of this coat of the artery. (Fig. 65.) This swelling of the intima is very characteristic. It is, in the earlier stage of the process, of a soft flabby consistence, and the lining membrane which is continuous over it can readily be stripped off, leaving the diseased tissue beneath. It thus contrasts strongly with the superficial patches of fatty degeneration which result from the passive metamorphosis of the endothelial and connective-tissue cells of the vessel. (See "Fatty Degeneration of Arteries.")

The results of the inflammatory process will depend upon its severity. If the process is very acute and the young elements accumulate rapidly, the intercellular substance becomes so completely destroyed, and the walls of the vessel so much softened, that dilatation, aneurism, or rupture ensue. Such acute changes, however, are comparatively rare. The inflammation is usually of less intensity and runs a more chronic course, and it is only to these more *chronic* arterial changes that the term "atheroma" is commonly applied.

FIG. 65.



Chronic Atheromatous Change in an Artery. Showing the new tissue in the deeper layers of the inner coat, and the consequent internal bulging of the vessel. In the darker portions the new tissue has become softened and pultaceous. At the lower part of the figure are seen a few of the most internal fibres of the middle coat. × 25. (Rindfleisch.)

When the process is less intense and more chronic in its course, it leads to various alterations in the wall of the vessel. The soft cellular infiltration of the deeper layers of the intima usually undergoes retrogressive changes, owing to deficient nutritive supply. These changes commence in the deeper portions of the new tissue. The young cells undergo fatty degeneration, the intercellular substance softens, and thus a soft, yellowish, pultaceous material is produced beneath the lining membrane of the vessel. This has been termed an *atheromatous abscess.* The lining membrane may ultimately give way and the softened matters be carried away by the circulation, and thus is produced the *atheromatous ulcer.* In other cases the more liquid constituents of the degenerated tissue gradually become absorbed, cholesterin forms, and thus a mass, consisting of broken-down fibres and cells, fatty débris, and cholesterin crystals, with a varying quantity of the original fibrillated tissue, remains in the deeper layers of the inner coat. (Fig. 65.) This may subsequently calcify and so form a *calcareous plate.*

In the most chronic forms of the atheromatous process there is but little softening of the new tissue, the cells become developed into a fibrillated structure, and thus is produced a *fibroid thickening* of the inner coat of the artery. The organization, however, is rarely complete, more or less fatty débris being usually enclosed in the fibroid stroma.

INFLAMMATION OF THE HEART—ENDOCARDITIS.

Inflammatory processes in the heart, although they sometimes occur in the muscular substance (Myocarditis), are for the most part met with in the endocardium. Here they closely resemble those occurring in the internal arterial coats which constitute atheroma. The endocardium and inner coat of an artery are very analogous in their structure, both being almost non-vascular and consisting of fibrous and elastic layers with an internal endothelial covering.

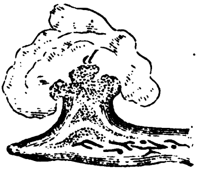
These processes in the endocardium are almost exclusively confined to the *left* cardiac cavities, and in the great majority of cases commence in, and comparatively rarely extend beyond, the confines of the aortic and mitral valves and the corresponding orifices. Further—it is those portions of the valves which come into contact in the act of closure, and are thus most exposed to friction, which are especially involved, and in which the changes usually commence. Thus, in the aortic valves, it is the convex surfaces of the segments which are most liable to be affected, and not the free edge of the segment, but the little band of tissue which passes from its attached border to the corpus Arantii in the centre; and in the mitral valve, the auricular surface of the segments at a little distance from the attachment of the chordæ tendineæ.

Endocarditis may be either *acute* or *chronic*. In both cases the process has its seat in the sub-endothelial tissue.

ACUTE ENDOCARDITIS.—If the process be acute, the deeper layers of the endocardium become rapidly infiltrated with young cells, and as these increase in number the intercellular substance becomes softened and destroyed, and thus is produced a soft tissue composed almost entirely of cells such as always results from inflammatory processes in connective tissue. The new tissue as it increases tilts up the superjacent endothelium and projects in the form of minute granulations and vegetations upon the surface of the softened valve. The endothelial elements may also participate in the active process.

The above changes take place in an almost non-vascular tissue, and although there is more or less increase of vascularity in the more external endocardial layers, where *the capillaries* are more numerous, there is rarely any redness or injection of the endocardium seen after death. Neither is there usually any liquid exuded upon the surface of the granulations. What was formerly regarded as an exuded material, is in the main coagulum, which has been deposited from the blood upon the roughened surface of the valve. This deposition of coagulum frequently occurs in endocarditis, the roughened and abnormal endocardium acts as a foreign body and so causes a deposition upon its surface. This must not be confounded with the vegetations themselves. (Fig. 66.)

FIG. 66.



Acute Endocarditis. A granulation from the mitral valve, showing a fibrinous coagulum upon the surface of the granulation. × 10. (Rindfleisch.)

If the inflammatory process is very acute the whole of the new tissue may break down, and thus a loss of substance result—an *endocardial ulcer.* This takes place without any accumulation of cells sufficient to form an abscess, the new tissue simply becoming rapidly softened and disintegrating. In rare cases, however, small quantities of pus are found in the deeper endocardial layers. The ulcer is irregularly defined, and its edges are usually swelled and thickened. This ulceration may lead to perforation of the valve, or to a considerable destruction of its substance. Laceration or aneurism may also ensue from the pressure exercised by the blood against the damaged tissue.

If the process be less severe, and the distintegration of the new tissue less complete, the latter becomes incompletely organized into a fibrillated structure, whilst it undergoes, in part, fatty and calcareous degeneration. These changes may result in the adhesion of the valves, either to one another or to the walls of the heart. They always produce permanent thickening, rigidity, and shrinking of their structure. The new tissue may continue to grow after the severity of the process has subsided, and thus are produced the vegetations and papillary excrescences on the valves which are so commonly met with. These consist of a lowly-organized tissue, which tends quickly to undergo fatty and calcareous changes.

CHRONIC ENDOCARDITIS.—This may be the sequel of acute inflammation, or the process may from its commencement be chronic in its nature. In chronic endocarditis the formation of new cells is much less rapid and abundant than in the acute form; the intercellular substance consequently becomes much less softened and destroyed, and the new tissue has a much greater tendency to become developed into a fibrillated structure. The extent to which the new tissue becomes organized, however, varies. It may undergo partial retrogressive changes, and thus a loss of substance result (ulceration); or the organization may be more complete and lead to a *fibroid thickening* of the endocardium. In the latter case considerable induration and contraction of the valves or valvular orifice will result. The new tissue frequently forms papillary growths on the valves, which undergo partial fatty and calcareous changes.

FIBROID INDURATION OF THE HEART.

Fibroid induration of the heart, although alluded to by other observers, was first brought prominently under the notice of English pathologists by Dr. Quain.* The change consists in the development of a fibrillated tissue between the muscular elements. The process commences in the intermuscular septa around the blood-vessels. This becomes infiltrated with small cells which tend to become developed into a fibrillated structure. (Fig. 67.) The growth of new tissue gradually extends between the bundles of muscular fibres, so that ultimately each fibre

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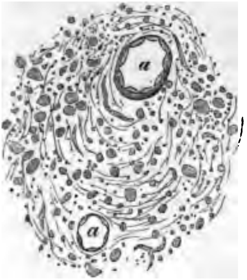
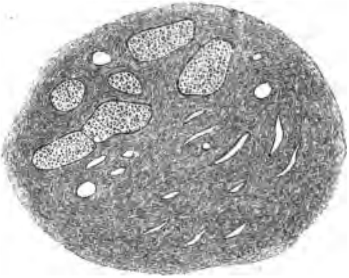
* *"Lectures on Diseases of the Walls of the Heart."* Lancet, *March, 1872.*

FIG. 67.



Fibroid Induration of the Heart. A thin section from the wall of the left ventricle, showing the small-celled growth in the intermuscular septa around the blood-vessels. *a. a.* vessels. × 200.

FIG. 68.



Fibroid Induration of the Heart. A section from the left ventricle of the same heart as Fig. 67, showing a more advanced stage. The fibroid tissue surrounds the individual muscular fibres, which are undergoing fatty degeneration. × 200.

may be surrounded by a tract of dense fibroid tissue. (Fig. 68.) The muscular fibres themselves, owing to the resulting interference with their nutritive supply, atrophy and undergo fatty metamorphosis. (Fig. 68.)

Fibroid induration of the heart appears in most cases to be induced by inflammatory processes commencing in the peri- or endo-cardium. When secondary to pericarditis, the change is always most advanced in the more external portions of the cardiac walls, and it usually affects both the right and left ventricles. When, on the other hand, an endocarditis is the precursor of the indurative process, the change is most marked in the more internal muscular layers, and inasmuch as inflammatory processes in the endocardium occur almost exclusively in the left cardiac cavities, the left ventricle is principally involved.

Although the growth of new tissue is thus usually most advanced either in the more external or in the more internal portions of the muscular walls, it is by no means uniformly distributed. In some parts it may be very dense, the muscular fibres being entirely obliterated, whilst in others it is almost entirely wanting, and the muscular elements present a normal appearance.

Fibroid induration of the heart appears to occupy the same pathological position as similar fibroid changes in other organs—*e.g.*, in the liver and kidneys. It must therefore be regarded as the result of a chronic inflammatory process, which might be termed *chronic myocarditis*. Its effect must evidently be to interfere very materially with the motive power of the organ, and it consequently constitutes one of the most grave of all cardiac diseases.

The cardiac walls become much thickened by the new growth, and the induration of texture is often very considerable. In the specimen from which the accompanying drawings were made, the disease was apparently secondary to an *endocarditis*, and the walls of the left ventricle were *so hard that they* cut almost like a piece of tendon.

CHAPTER XXXI.

INFLAMMATION OF LYMPHATIC STRUCTURES.

INFLAMMATORY processes in lymphatic structures usually result from their irritation by substances conveyed to them by the lymphatic vessels. They include—*acute* and *chronic* inflammations, and the specific inflammation associated with *Typhoid Fever*. Each of these must be considered separately.

ACUTE INFLAMMATION OF LYMPHATIC STRUCTURES.

Examples of acute inflammation of lymphatic structures are furnished by the inflammation of the glands in the axilla from a wound on the hand, of the glands in the groin from gonorrhœa, and of Peyer's and the solitary glands in the intestine from inflammation of the intestinal mucous membrane.

The process consists in a hyperæmia of the gland together with a rapid increase in the number of the lymph-corpuscles. This increase is probably due, partly to a hyperplasia of the original cells of the gland, and partly to the migration of blood-corpuscles. The corpuscles not only increase in number, but many of them become much larger in size, and their nuclei multiply. The cells of the trabeculæ also participate in the active process. The increase in the size of the elements and the multiplication of their nuclei usually leads to the production of some larger cells containing three or four nuclei. These resemble the "myeloid cells." They have been already alluded to as being frequently met with in lymphatic structures which are undergoing active processes. (See Fig. 35.) Owing to these changes the gland becomes considerably increased in size, soft and pulpy in consistence, and its cortical and medullary parts are no longer distinguishable.

Upon the removal of the source of irritation the process may gradually subside, the new elements undergo disintegration and absorption, and the gland return to its normal condition (Resolution). In other cases the process goes on to suppuration, the trabeculæ are destroyed, many of the cells become disintegrated, and the loculi of the gland become filled with pus. This is usually associated with inflammation and suppuration of the surrounding connective tissue. In the glands of a mucous membrane the process gives rise to what is known as a follicular abscess.

CHRONIC INFLAMMATION OF LYMPHATIC STRUCTURES.

Chronic inflammations of lymphatic structures result from irritations which are less severe and more prolonged in their action than those which give rise to the acute form. The resulting hyperplasia of the elements of the gland is consequently a more continuous one, and the gland becomes more or less permanently increased in size. This hyperplasia takes place not only in the lymph-corpuscles, but also in the reticulum. These chronic imflammatory processes differ from the acute, inasmuch as they lead to a gradually increasing development of the reticular structure of the gland. The reticulated network becomes thicker and more fibrous, its meshes become smaller and smaller, the lymph-corpuscles diminish in number, and thus the gland *becomes hard* and fibrous in consistence.

In those chronic inflammations of the lymphatic glands which occur especially in scrofulous subjects, and in which the glands tend to become caseous, the process more closely resembles in its histological details what has been described as occurring in the acute form. Here the proliferation is principally confined to the lymph-corpuscles. These increase in number, and many of them become considerably enlarged and form multinucleated elements. The gland thus becomes enlarged, soft, and elastic in consistence, and of an uniform greyish-white colour. Owing to the obstruction to the circulation caused by the pressure of the new growth, the latter undergoes retrogressive changes and becomes caseous. The caseous material may subsequently liquefy, or become infiltrated with calcareous particles.

INFLAMMATION OF LYMPHATIC STRUCTURES IN TYPHOID FEVER.

The inflammatory processes which occur in the lymphatic structures in Typhoid Fever, have their seat in the spleen, in the lymphatic structures of the intestine, and in the mesenteric glands.

The Spleen.—In the spleen the change resembles that which occurs in many of the other acute febrile diseases, although it reaches its maximum in typhoid. The spleenic tissue becomes exceedingly vascular, and the lymphatic elements increase rapidly in number, so that the organ often attains two or three times its natural size. Many of the new elements enter the blood, thus causing a slight temporary increase in the number of white blood-corpuscles. As the fever subsides, the hyperæmia diminishes, the hyperplastic process ceases, many of the new elements undergo disintegration and absorption, the remainder enter the blood, and thus the organ again attains its normal characters and dimensions.

The Intestinal Lymphatic Structures.—It is in the solitary and Peyer's glands that the most characteristic changes take place in typhoid fever. These structures may be involved throughout the whole of the small and large intestine, but in most cases the process is limited to those in the ileum and cæcum; and those glands are always the most affected which are situated the nearest to the ileo-cæcal valve.

The primary change here consists in an increase in the vascularity of the glands, and in a general proliferation of their lymphatic elements. Many of the elements also increase considerably in size, so as to form the multinucleated cells already alluded to. Both Peyer's patches and the solitary glands thus become considerably enlarged and prominent, standing up above the surface of the intestine. They are of a greyish-white or pale reddish colour, and of a soft, brain-like consistence. The surrounding mucous membrane is also exceedingly vascular, and is the seat of an acute catarrhal process. This catarrh is more or less general, and usually precedes the swelling of the glands. The new growth, in many parts, rapidly extends beyond the confines of the glands into the immediately surrounding and subjacent tissues, and even in some cases into the muscular coat. It may thus be said to become heteroplastic.

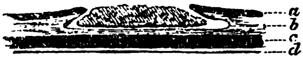
The process now passes into the second stage—that of the death and disintegration of the newly-formed tissue. This may terminate in various ways. The enlarged glands, many of them, subside, the new elements become disintegrated and are absorbed, and the gland thus undergoes a gradual process of resolution. In others, the individual follicles of the gland rupture discharging their contents externally, and the patches then acquire a peculiar reticulated appearance. The most characteristic termination, however, of the typhoid process, is the separation of the dead tissue as a slough, and the formation *of the typhoid ulcer.*

The process of sloughing and ulceration may, like that of proliferation, take place uniformly throughout the whole gland, in which case the whole mass is thrown off, leaving an ulcerated surface corresponding in size with that of the gland. More commonly, however, in the patches, the sloughing commences in different portions of the patch, and small irregular losses of substance result which may gradually extend until they form one large ulcer.

Although, as already stated, the new growth may extend beyond the confines of the glands, this is rarely the case with the ulceration. The heteroplastic growth undergoes resolution, and hence the ulcers have the same configuration as the original glands; those originating from the patches being oval, with their long diameter in the direction of the gut; and those originating in the solitary glands being spherical in shape. In rare cases, when there is much infiltration of the surrounding mucous membrane, the ulceration may extend slightly beyond the confines of the glands.

With the sloughing and disintegration of the new tissue the process of proliferation ceases, and hence there is no induration or thickening of the base or edges of the ulcer. The base is smooth, and is usually formed of the submucous or muscular coat of the intestine. The edges are thin and undermined, and consist of a well-defined fringe of congested mucous membrane. (Fig. 69.) This is best seen when the gut is floated in water. In

FIG. 69.



A Typhoid Ulcer of the Intestine (diagrammatic). Showing the undermined edges of the ulcer, and the slough still adherent. *a.* Epithelial lining. *b.* Submucous tissue. *c.* Muscular coat. *d.* Peritoneum.

some cases, however, the sloughing extends deeper, through the muscular layer to the sub-peritoneal tissue, and it may thus cause perforation and peritonitis.

The third stage of the process is that of cicatrization. This takes place by the resolution of the peripheral heteroplastic growth, the approximation and union of the undermined edges with the floor of the ulcer, and the gradual formation from the margin of an epithelial covering. The gland-structure is not regenerated. The resulting cicatrix is slightly depressed, and less vascular than the surrounding mucous membrane. There is no puckering or diminution in the calibre of the gut. In some cases, however, cicatrization does not take place so readily, and the floor of the ulcer becomes the seat of a *secondary* ulceration. This usually takes place after the general disease has run its course, or during a relapse. Profuse hæmorrhage and perforation more commonly result from this secondry ulceration than from the primary sloughing of the glands.

The Mesenteric Glands.—The change in the mesenteric glands is probably secondary to that in the intestine. These glands become the seat of an acute hyperplasia, and are enlarged, soft, and vascular. They usually, like many of the glands in the intestine and the spleen, undergo a gradual process of resolution. In rare cases, however, the capsule of the gland is destroyed, and the softened matters may escape into the peritoneal cavity and so cause peritonitis. The enlarged glands may also become caseous, and subsequently calcify.

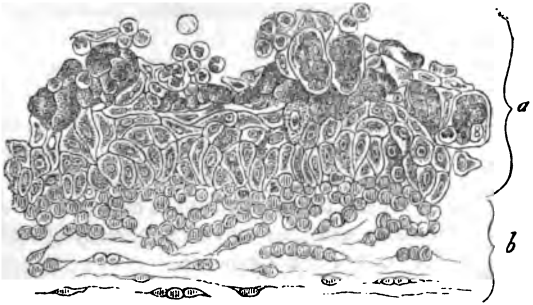
CHAPTER XXXII.

INFLAMMATION OF MUCOUS MEMBRANES.

In mucous membranes inflammatory processes are divided into *catarrhal*, and *croupous* or *fibrinous* inflammations.

Catarrhal Inflammation.—Catarrhal inflammation, or as it is more commonly called *catarrh*, is much the more frequent. In its milder forms this is characterized mainly by an increased secretion of mucus. A hyperæmia of the membrane is followed by an abnormal production of epithelial and mucous elements. The liquid which transudes from the blood-vessels is more abundant, the small, spherical, newly-formed cells which constitute the mucus-corpuscles are produced with increased rapidity, and the result is an increased secretion of mucus rich in corpuscular elements. These young cells are many of them emigrant blood-corpuscles, others are produced within the epithelial cells by endogenous multiplication. As the proliferation continues, many of the epithelial elements become loosened and are discharged with the mucus, and within these groups of bodies may occasionally be seen, which are evidently young mucus-corpuscles. (Fig. 70.) The secretion of the mucous glands is also increased. Owing to these changes, the mucous membrane becomes swelled and abnormally vascular. The increased vascularity is evidenced by redness during life, but after death the blood usually passes out of the vessels, and the membrane may look paler than natural.

FIG. 70.



Catarrhal Inflammation of the Conjunctiva. *a.* Epithelium. *b.* Sub-epithelial connective tissue. Showing the proliferation of the epithelium, and the origin of the young elements within the epithelial cells. (Rindfleisch.)

If the irritation be more severe, the vascular phenomena are more marked, the production of young elements is more rapid, they are smaller and not so well developed, the epithelium loosens and falls off more readily, and the secretion becomes puriform from the great number of corpuscular elements which it contains. Many of these elements are indistinguishable from pus-corpuscles, others are somewhat larger and resemble the corpuscles of normal mucus. Between the corpuscles of mucus and pus there is no line of demarcation, the one passing by insensible gradations into the other. The former are somewhat larger and more regular in shape than the latter, and usually contain only a single nucleus. As the process continues the sub-epithelial tissue is gradually involved, and becomes infiltrated with young cells. Owing to the loss of epithelium, the surface of the membrane may at the same time become more or less irregular, and *present numerous irregular* abrasions or ulcers.

These changes in the mucous membrane itself are accompanied by a hyperplasia of the lymphatic structures which it contains. The lymph-follicles become enlarged from the multiplication of their elements. Their contents may soften and form a minute pseudo-abscess, and this bursting gives rise to a small ulcer. These are the follicular ulcers so often seen in catarrhal conditions of the intestines and pharynx. The ulceration in some cases extends beyond the confines of the follicle. The proper glandular structures may also become involved. Their epithelium multiplies, the glands become choked with the epithelial elements, and they may subsequently atrophy. This is seen in catarrh of the stomach.

The acute process may quickly subside, or it may become chronic. In the latter case the vascularity diminishes, but the multiplication of elements continues both in the epithelial and sub-epithelial tissue, as does also the increased secretion of mucus (suppuration); the latter thus becomes thicker and more puriform in character.

Chronic catarrhal inflammations of mucous membranes differ from the acute, inasmuch as the sub-epithelial connective tissue is much more extensively involved. This tissue becomes infiltrated with young elements which may ultimately form a more or less completely fibrillated structure. The membrane thus becomes indurated and thickened, and the pressure exercised by the new tissue may induce atrophic changes in the glandular structures which it contains; by preventing the exit of their secretion it may also cause them to dilate so as to form cysts. This atrophy of the proper glandular structures is seen in chronic catarrh of the stomach. These changes in the sub-epithelial connective tissue are usually accompanied by enlargement of the lymphatic structures, an enlargement which sometimes gives to the membrane a *nodular* or granular appearance: this is well seen in the *pharynx* (follicular pharyngitis). The enlarged lymphatic structures may also constitute the starting-points of an ulcerative process. (See "Tuberculosis of Mucous Membranes.") In some situations, as the stomach and intestine, the membrane often at the same time becomes deeply pigmented.

CROUPOUS OR FIBRINOUS INFLAMMATION.—This is a more intense form of inflammation than the preceding, and is characterized by the exuded liquids containing so large a proportion of fibrinogenous substance and albumen that they coagulate within and upon the surface of the membrane. Fibrinous inflammation may be induced artificially by severe irritants, and it occurs in croup, diphtheria, and in some cases of dysentery.

At its commencement the process is simply a severe catarrhal one, consisting in an increase in the vascularity of the membrane, together with an exudation of liquor sanguinis and blood-corpuscles, and proliferation of the epithelial elements. The proportion of fibrinogenous substance and albumen exuded, however, is much greater than in the less severe catarrhal inflammation, and these coagulate more or less completely within and upon the surface of the membrane, enclosing as they do so the innumerable newly-formed cell-structures.

Croup.—In croup the exuded materials coagulate principally upon the surface of the membrane, where, together with the newly-formed cellular elements, they form the *false membrane.* This, which can readily be removed from the subjacent epithelial layers, consists of amorphous or finely fibrillated fibrin enclosing innumerable epithelial cells and pus-corpuscles. In consistence it varies considerably, being in some cases firm and tough, in others soft and amorphous. After its removal, the membrane is left partially deprived of its epithelium. If the process subsides the epithelium is reproduced and the part returns to its normal condition; but if it continues, a *fresh false membrane* is formed. As the inflammation extends downwards into the trachea and bronchi, a gradual transition may often be observed from croupous to catarrhal inflammation. In the upper part of the air passages, where the process is most intense, the exudation is fibrinous, but in passing downwards, where it becomes less severe, the membrane is simply coated with mucus.

Diphtheria.—In diphtheria, the exuded liquids also contain a large proportion of coagulable material. The textural change differs, however, from that in croup, inasmuch as the submucous tissue becomes more extensively involved, and the liquids coagulate not only upon the surface but also within the substance of the membrane, so that the exudation cannot be so readily removed. The pressure exercised by the exuded substances and by the new growth, interferes with the circulation, and so causes the death and sloughing of portions of the membrane; the slough, after it has separated, leaving a considerable loss of substance.

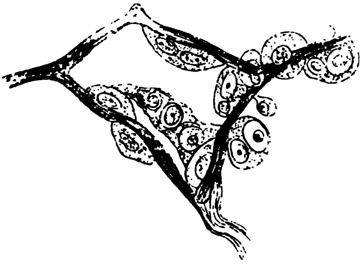
CHAPTER XXXIII.

INFLAMMATION OF SEROUS MEMBRANES.

INFLAMMATORY processes in serous membranes vary in their intensity, and in the amount and character of the effusion.

The process commences, as in mucous membranes, with hyperæmia, exudation of liquor sanguinis and emigration of blood-corpuscles, together with increased activity of the endothelial elements. The endothelial cells enlarge and become more granular, their nuclei multiply, and thus several new elements are formed within a single cell (*endogenous* multiplication) from which they

FIG. 71.

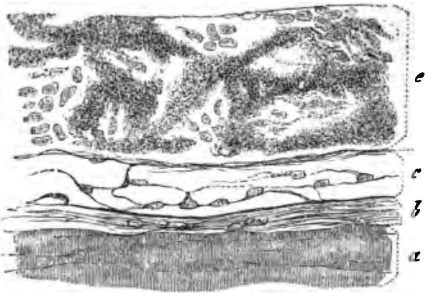


Inflamed Epiploon of a Rabbit. Showing the endogenous proliferation of the endothelium. × 250. (Cornil and Ranvier.)

subsequently escape, and in this way a number of new cells are produced. (Fig. 71.) The small, round, newly-formed elements, together with some of the older cells and a large number of emigrant blood-corpuscles, escape with the exuded liquor sanguinis into the serous cavity, where they may continue to exhibit their formative activity.

Owing to these changes the membrane loses its natural smooth and glistening appearance, and becomes opaque, roughened, and exceedingly vascular. Its surface at the same time becomes covered with a fibrinous layer, and more or less liquid transudes into its cavity. The material which exudes from the vessels and subsequently coagulates, exists as a soft, elastic, membranous, or reticulated investment, either gluing the two surfaces of the membrane together, or, if they are separated by liquid effusion, forming a slightly adherent layer. (Fig. 72.) The exuded liquid varies considerably in amount and is always turbid, thus differing from non-inflammatory effusions. It contains flakes and masses of coagulated

FIG. 72.



Inflammation of the Diaphragmatic Pleura. Showing the adherent fibrinous layer. *a.* Muscular coat of diaphragm. *b.* Sub-serous tissue. *c.* Serous membrane. *e.* Fibrinous layer. × 400. (Rindfleisch.)

fibrin and innumerable cell-structures, the latter being in the earliest stages of the process almost entirely emigrants. Similar elements are embedded in the adherent fibrinous layer.

The nature of the subsequent changes will depend upon the intensity of the inflammation, and upon the amount of liquid exuded into the serous cavity. If the inflammatory process subsides, and the liquid exuded is not sufficient to prevent the two surfaces of the membrane from coming into contact, they grow together and form an adhesion. This constitutes the so-called *adhesive inflammation.* The union is effected by the formation of connective tissue. The small round cells embedded in the fibrinous layer become elongated and spindle-shaped, the fibrinous material fibrillates, and numerous new vessels are formed. Many of the latter atrophy and disappear as the organization becomes complete. The process is thus precisely similar to that which takes place in the union of an incised wound. It is probable also that in some cases union may take place without the intervention of any fibrinous layer, by the formation and growing together of irregular papillary outgrowths from the subendothelial tissue.

If, however, the inflammatory process is severe, or the surfaces of the membrane are separated by a large quantity of liquid effusion, organization and adhesion cannot be thus readily effected. If a large quantity of liquid exists in the serous cavity, the removal of this becomes necessary before union can take place. If the inflammatory process continues, or its severity is great, union is prevented by the formation of pus. These two conditions must be considered separately.

The existence of a large amount of effusion interferes with the adhesion of the serous surfaces, and before this can be effected the absorption of the liquid becomes necessary. In some cases this occurs very rapidly. More frequently, however, the process is more prolonged, and the sub-endothelial connective tissue becomes involved before absorption takes place. When this is the case the connective tissue of the serous membrane becomes infiltrated with young cells, which form a granulation-tissue beneath the layer of proliferating endothelium. The endothelium itself gradually becomes less abundant, and the fibrinous exudation undergoes fatty changes and liquefies. The new granulation-tissue becomes exceedingly vascular from the formation of numerous blood-vessels, and if the inflammation subsides, it gradually developes into connective tissue, and thus a false membrane is formed rich in vessels which takes the place of the endothelial layer. As the liquid is absorbed, the two surfaces of the membrane come into contact and grow together, the new vessels becoming gradually obliterated.

If the inflammatory process does not subside, or from its commencement is of considerable severity, it is attended by the formation of large quantities of pus. In this case the emigration of blood-corpuscles is so considerable that the young elements exist in large enough numbers to give to the exuded liquids a puriform character. The effusion is then termed *purulent* (empyema). As the connective tissue becomes involved and a granulation-tissue is formed, this may continue to generate pus like an ordinary granulating wound. If the pus be removed, the suppuration may gradually cease, the granulation-tissue develop into a fibrous structure, and the union of the serous surfaces thus be effected. The serous membrane becomes greatly thickened, and the new tissue undergoes considerable contraction in the process of its organization.

CHAPTER XXXIV.

INFLAMMATION OF THE LIVER.

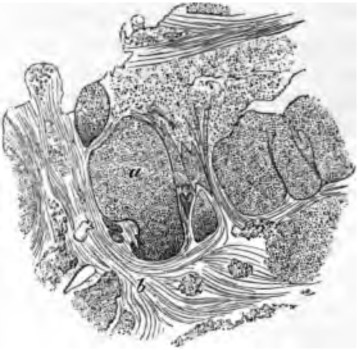
INFLAMMATORY processes in the liver are either acute or chronic. *Acute* inflammations, leading to suppuration, are usually infective in their nature, resulting from the transmission of infective materials from inflammatory lesions in the abdominal organs or in other parts. The processes are consequently most frequently disseminated and confined to small portions of the hepatic substance. The pus-corpuscles—which usually accumulate so as to form an abscess—are almost entirely emigrants, although recent investigations render it highly probable that they may also originate by the endogenous proliferation of the liver-cells.

Chronic inflammatory processes in the liver, being of much less intensity, lead to a gradual increase in the connective tissue of the organ, and consequently to induration and to the subsequent atrophy of its proper structure. They constitute what is known as *interstitial hepatitis*, or more commonly as *cirrhosis.*

CIRRHOSIS OF THE LIVER.

Cirrhosis of the liver, or interstitial hepatitis, is characterized by a gradual increase in the connective tissue of the organ and by subsequent atrophy of the liver-cells, so that *when examined* with a low magnifying power, the acini are seen to be separated by broad tracts of new interstitial growth. (Fig. 73.)

FIG. 73.

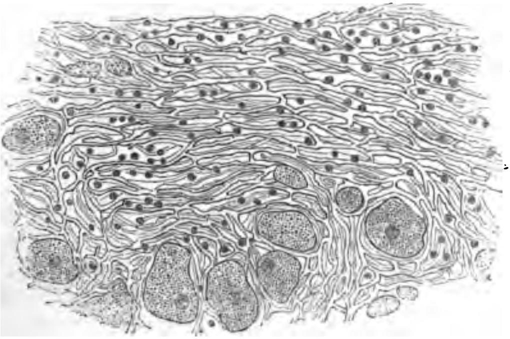


Cirrhosis of the Liver. Showing the growth of connective tissue between the hepatic lobules. *a.* Lobules. *b.* New growth of interlobular connective tissue. × 16.

The process usually commences in the connective tissue surrounding the smaller branches of the portal vein, and gradually involves that surrounding the larger ones, until ultimately the connective tissue throughout the whole organ may become involved. This tissue becomes infiltrated with small round cells, from which are produced a more or less completely fibrillated structure, containing in the earlier stages of its development numerous new blood-vessels which are supplied by branches of the hepatic artery. The change is rarely uniform, but is much more advanced in some parts than in others. In many places the new tissue consists almost entirely of cells, whilst in others the fibrillation is much more marked, or the growth forms a network of homogeneous bands within the meshes of which the cellular elements are grouped. In short, the vascular and richly cellular growth gradually assumes the characters of cicatricial tissue, the vessels at the same time becoming obliterated. (See Fig. 63.)

The effect of the new growth is ultimately to cause atrophy of the hepatic cells, and to obstruct the circulation through the portal capillaries and the passage of bile through the bile-ducts. This effect is materially increased by the process of contraction which the new tissue undergoes. The hepatic cells in the outer zone of the lobules are the first to atrophy; the new tissue insinuating itself between them, so as to gradually involve the intercellular network. (Fig. 74.) The cells then become smaller and undergo fatty metamorphosis; and ultimately they are completely destroyed. Those in the central parts of the lobule are in the earlier stages but little altered, although they are often stained with bile. As the growth extends, however, these also become annihilated, and the whole lobule is *replaced by connective* tissue. The cells in the

FIG. 74.



Cirrhosis of the Liver. A thin section from the external portion of one of the hepatic lobules. Showing the new growth of connective tissue, and the way in which it involves the intercellular network and causes atrophy of the liver-cells. × 200.

outer part of the lobules are sometimes infiltrated with fat prior to their destruction, the cirrhosis being associated with fatty infiltration.

The obliteration of the portal capillaries by the new tissues gives rise to ascites, hæmatemesis, diarrhœa, enlargement of the spleen, and to the other results of portal congestion. Obstruction of the bile-ducts, although it may cause staining of the hepatic substance, is rarely such as to interfere with the passage of the bile into the intestine, and hence there is usually but little general jaundice.

Physical characters.—The liver in the early stages of cirrhosis is usually slightly enlarged, the enlargement being almost uniform. In some cases the increase in size may be considerable. The edge is rounded and thickened. If the new tissue is very rapidly produced, the consistence may be somewhat diminished; much more commonly, however, the organ is from the first tougher than natural and breaks down less readily under the finger. The characters which it subsequently presents depend upon the distribution of the new tissue. If this is uniform, there will be a gradual and almost uniform diminution in size, and the surface and shape will be but little altered. If on the other hand, as is much more frequently the case, the new tissue is more abundant in some parts than in others, or undergoes irregular contraction, the resulting atrophy will be correspondingly irregular and the surface of the organ will be granular and nodular. In the later stages, the liver is exceedingly firm, dry, tough, and fibrous. On section, the new tissue is visible to the naked eye surrounding the lobules and in many parts completely replacing them. This gives to the cut-surface a mottled granular appearance, the lobules themselves contrasting with the new interlobular tissue; and this appearance is sometimes increased by fatty infiltration of the cells in the peripheral zone. The capsule also may be thickened, and the organ is sometimes stained with bile.

CHAPTER XXXV.

INFLAMMATION OF THE KIDNEY.

INFLAMMATORY processes in the kidney present certain variations according to their intensity. They comprise *suppurative, tubal,* and *interstitial* nephritis. Of these, suppurative nephritis, as the name implies, is an intense inflammation leading to the formation of abscess. It usually results from the transmission of infective materials from some primary lesion, and it consequently belongs to the class of infective inflammations. Tubal nephritis is also an inflammation of considerable intensity, but much less so than the suppurative variety. In it the structural changes have their principal seat in the tubular epithelium. Interstitial nephritis is an inflammatory process which runs a more chronic course, and is of less intensity than either of the preceding. Consequently in it the principal structural changes take place in the connective tissue around the blood-vessels—in the intertubular connective tissue. (See "Chronic Inflammations.") It must, however, be distinctly borne in mind that these two varieties of anatomical changes—those in the tubular epithelium and those in the intertubular connective tissue—are very frequently associated. Tubal and interstitial nephritis cannot therefore be separated from one another by any distinct line of demarcation. They might, perhaps, be more correctly designated *acute* and *chronic nephritis.*

SUPPURATIVE NEPHRITIS.

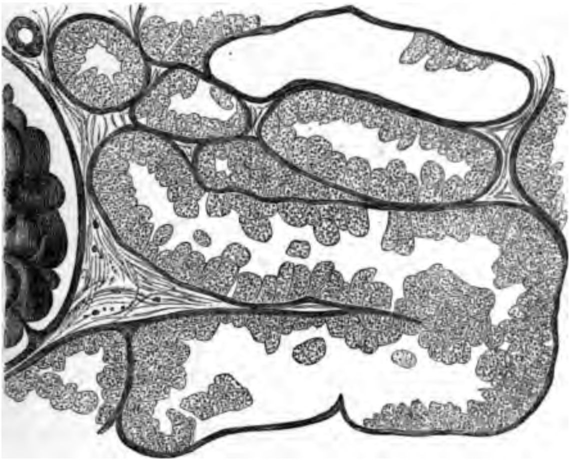
Acute inflammatory processes in the kidney attended by the formation of pus, give rise to *renal abscesses.* Such processes, as already stated, are usually infective in their nature, resulting from the transmission of infective materials from some primary lesion. They are for the most part associated with inflammation of the pelvis of the kidney, such as is produced by a renal calculus; or with those inflammatory changes in the mucous membrane of the urinary tract which result from vesical calculus, urethral stricture, or enlargement of the prostate. They are also met with in pyæmia. The resulting suppurative processes—as is usually the case in infective inflammations—are consequently disseminated, and numerous abscesses are thus formed in the substance of the organ. These abscesses are often surrounded by a zone of hyperæmic tissue. They may gradually coalesce, and so form one large abscess occupying the greater part of the kidney substance.

TUBAL NEPHRITIS.

Tubal nephritis, or as it is also called acute desquamative nephritis, is one of those morbid processes which constitute Bright's disease, of which it is the most common *acute* variety. The process, which has its seat mainly in the cortex, comprises an increase in the vascularity of the organ, exudation into the urine tubes, and swelling and proliferation of the tubular epithelium.

The earliest change in the organ consists in an inflammatory hyperæmia, accompanied by exudation into the urine tubes. Many of the capillaries at the same time frequently rupture, and thus there is an escape of blood-corpuscles and of liquor sanguinis into the tubes of the cortex; hence the blood and "blood-casts" in the urine which are so characteristic of the early stage of the disease. This hyperæmia and exudation are followed by swelling and proliferation of the epithelium in the cortical tubes. (Fig. 75.) The epithelial elements become swollen

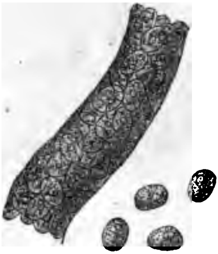
FIG. 75.



Tubal Nephritis. The earlier stage of the process. Showing the swelling of the tubular epithelium. In some of the tubes the epithelium has fallen out during the preparation of the section. × 200.

and granular. The granules, which are often so numerous as to occlude the nucleus of the cell, are probably albuminous matters which have been taken up by the protoplasm. They are soluble in acetic acid, and thus differ from molecular fat. This is the condition known as "cloudy swelling." The enlarged and granular epithelial cells may then proliferate, and thus new elements are produced. These, together with the older cells, which become loosened, accumulate within and distend *the tubes of* the cortex (Fig. 76), and some of them are washed away and appear in the urine as "epithelial casts."

FIG. 76.



Tubal Nephritis—a Single Urine Tube. Showing the accumulation of epithelial elements within the tube. In the few cells which have escaped is seen the granular condition of the protoplasm. × 350.

Owing to these changes the organ becomes considerably increased in size and exceedingly vascular. The capsule separates readily, exposing a perfectly smooth but very vascular surface. The consistence is diminished, the tissue breaking with a soft friable fracture. On section, the increase in the size of the organ is seen to be principally due to the increased thickness of the cortex. This is either of a reddish-brown, or of an opaque-white or pale buff colour; these differences depending upon the relative proportion of blood and of accumulated epithelial elements. Although in the earliest stage the colour is redder than natural, it usually soon becomes pale and opaque. This is owing to the swelling of the epithelial elements and to their accumulation in the cortical tubes. The blood becomes expressed from the intertubular vessels, and hence the increased vascularity is most evident in the Malpighian corpuscles, beneath the capsule, and in the pyramidal portion of the organ. The Malpighian corpuscles stand out as prominent red points, and the pyramidal cones are of a deep red colour, thus contrasting strongly with the pale opaque cortex.

The termination of the process varies. The increased vascularity and epithelial proliferation may subside, and the newly formed elements passing away in the urine, the organ gradually return to its normal condition. This is the most common termination when the inflammation is the result of scarlet fever. In other cases the disease continues; and although the vascularity diminishes, the vitality of the epithelial elements becomes so much impaired from the inflammatory process that they undergo retrogressive changes. The cells then continue to come away with the urine, adherent to the casts, but instead of presenting the swelled granular appearance as in the earlier stage of the disease, they contain molecular fat. This fat gradually increases in amount as the degeneration proceeds, until ultimately the cells are destroyed and it appears as free molecules and granules on the tube-casts.

This fatty degeneration of the epithelium is attended by corresponding changes in the appearance of the organ. The redness diminishes, and the Malpighian corpuscles are less prominent. The enlarged cortex presents a uniform yellowish tinge, studded with minute yellowish-white streaks. This is owing to the presence of fat in the tubes of the cortex. This fatty stage, if only slightly advanced, may undoubtedly pass off. The degenerated cells are carried away by the urine, from those which remain in the tubes the fat is probably partially absorbed, the retrograde process gradually ceases, and the organ returns to nearly its normal size and condition.

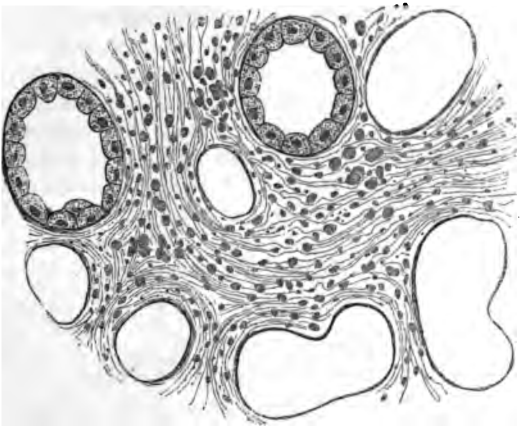
When the inflammatory process is of longer duration the intertubular connective tissue becomes involved. This tissue becomes infiltrated with small cells which ultimately tend to form a fibrillated structure. The new intertubular growth may gradually increase, and by its contraction lead to more or less irregular atrophy of the organ, such as will be described as occurring in interstitial nephritis. In other cases death ensues before any contraction takes place in the new intertubular material, and thus the organ may remain smooth and large to the termination of the disease. The intertubular growth is sometimes found thickly studded with fatty granules. These are probably derived from the epithelial elements, and their presence would appear to indicate that the products of the retrogressive metamorphosis of the tubular epithelium were undergoing a process of absorption.

INTERSTITIAL NEPHRITIS.

Interstitial nephritis, or as it is sometimes called granular degeneration of the kidney, occurs most frequently in the condition known as chronic Bright's disease. The process is usually chronic in its course, and is characterized, like the corresponding one in the liver, by a gradual increase of the connective tissue of the organ, and by the consequent atrophy of the tubal structures.

The first change in the kidney consists in an increase of the connective tissue between the urine tubes. In the earliest stages of the process the intertubular tissue becomes abnormally vascular and infiltrated with young cells. If the growth is very rapid, these may be exceedingly numerous, and the intercellular substance soft and amorphous. More commonly, however, the process is less acute and the cells less numerous, and the new tissue quickly tends to become developed into a fibrillated structure, the blood-vessels at the same time diminishing in number. This is the condition in which it is usually met with. (Fig. 77.) These changes are almost entirely limited to the cortical portion of the kidney, and although here they are more or less general, the new growth is more abundant in some parts than in others, being usually most so around the Malpighian bodies and in the neighbourhood of the capsule, with which it is closely united. In this stage the tubes and their epithelium are unaffected.

FIG. 77.

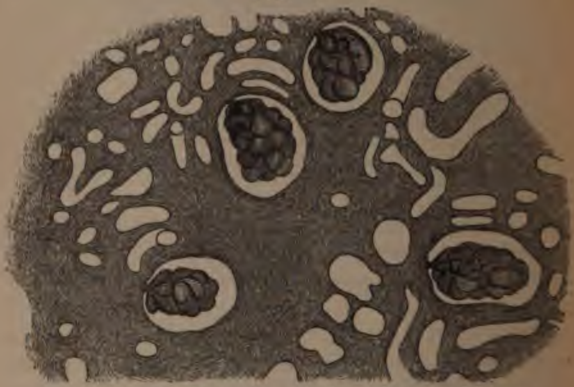


Interstitial Nephritis. The earlier stage of the process. Showing the cellular infiltration of the intertubular connective tissue. The epithelium has fallen out of some of the tubes during the preparation of the section. × 200.

In this early stage, the kidney is often somewhat increased in size, the capsule usually separates less readily than in health, and the surface of the organ is slightly granular. On section, the cortical substance is in some cases paler, in others redder than natural. The latter is the case when the process is secondary to mechanical congestion. The cut surface also looks obscurely granular. The Malpighian bodies stand out as red points, *and the bases* of the pyramids and surface of the organ are frequently hyperæmic. The consistence of the organ is usually slightly denser and tougher than natural. This, however, will vary with the character of the new tissue, as will also the increase in size and the irregularity of the surface. If the new tissue is slowly developed and consists principally of fibres, the size will be but little increased, whereas the increase in consistence and the granular condition will be more marked. If, on the other hand, the process be more acute, and the cellular elements predominate, there will be a greater increase in size, the granular character will be slight, and the consistence may be even softer than natural.

The second stage in the process is characterized by the atrophy of the tubular structures. (Fig. 78.) This is

Fig. 78.



Interstitial Nephritis. A very advanced stage of the process. Showing the large growth of dense fibrillated tissue between the tubes of the cortex, and the compression and atrophy of the tubes. The small amount of degenerated epithelium which was contained in some of the tubes has fallen out in the preparation of the section. × 50.

owing to the pressure exercised by the intertubular growth, and to the cicatricial contraction which it undergoes. The atrophy consequently is not uniform, but is more marked in some parts than in others. The organ gradually diminishes in size owing to the atrophy of the cortex, which may ultimately become almost completely destroyed. The blood-vessels become irregularly compressed, in many parts being entirely obliterated: their walls also become thickened. The tubes, like the vessels, are not uniformly affected. Many of them are unaltered or merely slightly dilated, whilst others become completely destroyed. The epithelium at the same time, owing to the interference with its nutritive supply, gradually undergoes retrogressive changes, so that it contains molecular fat. In the latter stages of the disease there is sometimes a proliferation of the epithelium. The irregular pressure exercised by the new growth also gives rise to the formation of cysts. These originate partly in the Malpighian capsules, and partly in the urine tubes—the latter becoming irregularly dilated.

In this more advanced stage the kidney is diminished in size. Its surface is more granular, the capsule more thickened and adherent, and it cannot be removed without tearing the kidney substance. The superficial vessels are seen unduly marked in the depressions between the granulations. The cortex is tough and fibrous, of a yellowish-grey or buff colour, mottled with yellow streaks and patches; and usually some small cysts are distributed throughout it. Calcareous deposits are also often seen as white streaks between the tubes of the pyramids.

When the change is the result of mechanical congestion the organs present somewhat different characters from those above described. The interstitial growth in the cortex takes place more uniformly, and hence the granular condition is less marked. The subsequent atrophy also is much less, and the appearance of the organs becomes altered from the large amount of blood which they contain.

CHAPTER XXXVI.

INFLAMMATION OF THE BRAIN AND SPINAL CORD.

INFLAMMATORY processes in the nervous centres are probably much less frequent than was formerly supposed. Many of those morbid changes in the brain and spinal cord which are attended by softening, and which were at one time regarded as the result of inflammation, are now known to owe their origin to simple interference with the vascular supply, such as results from embolism, thrombosis, or degenerative changes in the walls of the blood-vessels (see "Fatty Degeneration of the Brain").

The irritation which determines the occurrence of inflammation in the brain or cord is most frequently some external violence—a blow, simple concussion, or fracture of the osseous framework. In other cases it is diseased bone, as in the inflammation of the brain which so often results from disease of the petrous portion of the temporal bone.

The resulting inflammatory process is almost invariably limited to small portions of the cerebral or spinal substance. It is attended by the formation of pus, and usually leads to the formation of an *abscess*. The earliest change consists in intense and localized hyperæmia, which is frequently attended by rupture and minute extravasations of blood. The nervous tissue then becomes infiltrated with young cells and considerably softened, and it presents a uniform red or mottled colour. The nerve-fibres become disintegrated, and the nerve-cells may undergo fatty degeneration, thus forming the so called "inflammatory," or "exudation corpuscles" (see Fig. 5). In most cases the accumulation of young cells is sufficient to give rise to the formation of an abscess, and a yellowish or reddish puriform liquid gradually takes the place of the original softened mass. The tissue surrounding the abscess is also hyperæmic, softened, and infiltrated with cells. The abscess may gradually extend; much more commonly, however, it becomes limited and encapsuled by the formation of connective tissue from the neuroglia. When thus encapsuled, it may gradually dry up into a caseous or calcareous mass, or the absorption may be more complete so as to leave little more than a cicatrix. Respecting the source from which the young cells are derived—they are probably almost entirely emigrants, although they are possibly also partly the offspring of the cells of the neuroglia. The nerve-cells themselves appear to undergo no active changes in inflammation.

In addition to these localized and acute inflammatory processes, changes of a much more chronic nature, and often of a much wider and more general distribution—which are probably to be regarded as inflammatory—are met with in the nervous centres. These are characterized by a gradual increase in the connective tissue (neuroglia) and by atrophy and disintegration of the proper nervous elements.

INFLAMMATORY SOFTENING OF THE BRAIN.—Conditions of softening of the cerebral or spinal substance resulting from inflammation, other than those which have been above described, probably rarely, if ever, occur as *primary* lesions. Most varieties of softening which were formerly described as inflammatory—either from the red colour of the softened tissue or from the acuteness of the process—

result, as already stated, from embolism or thrombosis (see "Embolism in the Brain"), or are simply passive degenerative changes in which more or less extravasation of blood has taken place into the softened tissue (see "Fatty Degeneration of the Brain"). Inflammation and consequent softening of the nervous tissue, however, by no means unfrequently occurs as a *secondary* process. It takes place especially around clots of blood or other morbid products within the brain or spinal cord, and results from the injurious influence which these substances exercise upon the immediately adjacent structures. Such a result is not unfrequent in cases of cerebral hæmorrhage. The nerve-tissue immediately surrounding the clot becomes the seat of an inflammatory process, and it is found after death softened, hyperæmic, and infiltrated with young cells. Inflammation of the superficial portions of the cerebral and spinal substance also occurs as the result of meningitis.

CHAPTER XXXVII.

INFLAMMATION OF THE LUNGS.

In the lungs, inflammatory processes comprise the three following varieties:—*Croupous*, *catarrhal*, and *interstitial* pneumonia. Of these, the former occurs as an independent affection, whereas the two latter are almost invariably the result of some antecedent bronchial or pulmonary inflammation.

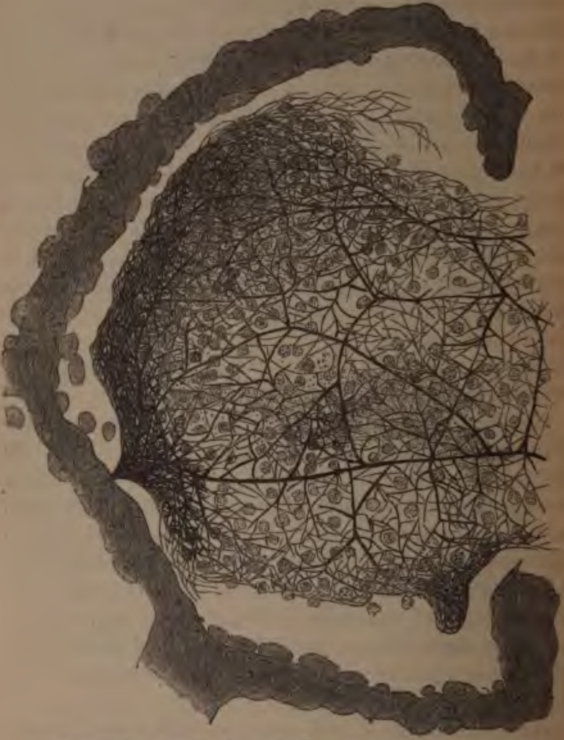
CROUPOUS PNEUMONIA.

Croupous, *exudative*, or *lobar* pneumonia, is characterized by intense inflammatory hyperæmia and by the exudation of a large amount of coagulable material into the pulmonary tissue. It is termed "croupous" because, like the croupous inflammation of mucous membranes, the exuded liquids contain a large quantity of fibrinogenous substance. This form of pneumonia almost invariably affects an extensive portion of the lung, hence the term "lobar" which is applied to it. The process is commonly described as consisting of three stages—1st, that of *engorgement;* 2nd, that of *red hepatization;* and 3rd, that of *grey hepatization.*

In the *first* stage, that of *engorgement*, the lung becomes exceedingly vascular, the changes in the blood-vessels and circulation being such as have been already described as characteristic of inflammation. The organ is of a dark red colour, its specific gravity and absolute weight are increased, its elasticity is diminished, it is less crepitant than natural, and pits upon pressure. Its cut-surface yields a reddish, frothy, tenacious liquid.

In the *second* stage, that of *red hepatization*, there is an

FIG. 79.

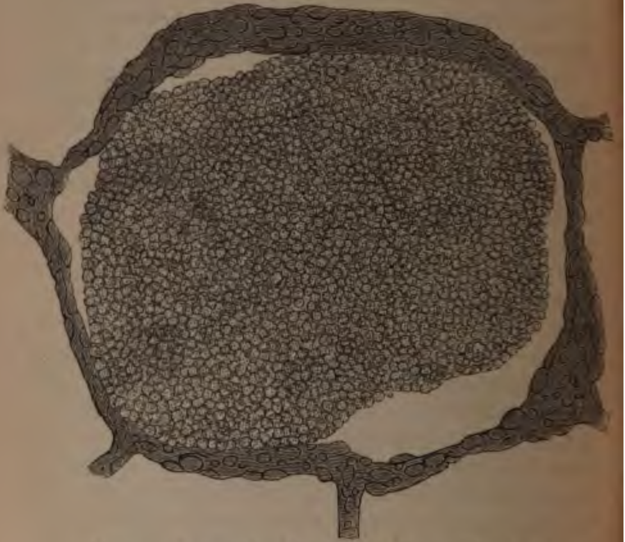


Croupous Pneumonia—Red Hepatization. Showing the fibrinous coagulum in one of the pulmonary alveoli, enclosing within its meshes numerous leucocytes, which are already commencing to undergo fatty metamorphosis. A few leucocytes are also seen in the alveolar walls, and the alveolar endothelium is swollen and granular. × 200.

exudation of liquor sanguinis and migration of blood-corpuscles into the pulmonary tissue. Some of the vessels may also rupture, and thus small extravasations occur. The exuded liquids coagulate within the air-vesicles and in the interstices of the interlobular tissue, the coagulum enclosing numerous white and some red blood-corpuscles. The lung is now much heavier than in the preceding stage. It contains but little or no air, usually sinks in water, and cannot be artificially inflated. It does not crepitate under the fingers, but is remarkably friable, breaking down readily with a soft granular fracture. The cut surface is of a dark reddish-brown colour, and it presents a granular appearance, the granules being the plugs of fibrinous coagulum contained in the air-vesicles. These granules also sometimes give to the reddish-brown organ a peculiar grey mottling. Throughout this stage there appears to be but little alteration either in the alveolar walls or in the alveolar endothelium. The former are often seen to contain a few leucocytes, and the latter may be somewhat swollen and granular. (Fig. 79.)

The *third* stage, that of *grey hepatization*, is characterized by a continuance in the emigration of leucocytes, and by cell-proliferation. The white blood-corpuscles continue to escape from the vessels, and thus their number within the alveoli gradually increases. It is probable that they may also increase by multiplication. The endothelial cells lining the alveolar walls, which were only swollen and granular in the earlier stage of the process, now undergo more active changes. Their nuclei enlarge and multiply, and ultimately numerous new young cells are produced, many of which are indistinguishable from the emigrant blood-corpuscles. The pulmonary alveoli thus become completely filled with young cell-forms, so that the fibrinous exudation is no longer visible as an independent material, as it is in the stage of red *hepatization*. (See Fig. 79.) These cells rapidly undergo retrogressive fatty changes, so that, as usually seen, the alveoli are filled with granular elements, which in many parts have lost their distinctive outlines. (Fig. 80.)

FIG. 80.



Croupous Pneumonia—Grey Hepatization. Showing the large accumulation of cellular elements within one of the pulmonary alveoli, which in some parts have undergone such extensive fatty degeneration that their distinctive outlines are no longer visible. × 200.

The alveolar walls, as in the preceding stage, contain a few leucocytes. The weight, density, and friability of the lung now become even greater than in the stage of red hepatization, although the granular aspect of the cut surface is much less marked. The tissue is now quite *soft* and pulpy, and a puriform liquid exudes from its cut surface. The most prominent feature, however, is the alteration which takes place in the colour of the organ. This gradually changes from a dark reddish-brown to a grey or yellowish-white. This is owing partly to the pressure exercised upon the blood-vessels by the exuded substances and newly formed cells, and partly to the fatty degeneration which the latter have undergone.

Such are the characteristic changes which occur in croupous pneumonia. In those very numerous cases, however, in which the pneumonia is secondary to some other disease, or occurs in debilitated subjects, the changes in the lung may present some deviations from those which have been above described. In these secondary pneumonias the exuded substances are often less abundant and less coagulable, and consequently the weight of the lung is much less increased. The organ is also less dense and friable than when the process occurs in a healthy person. The existence of much œdema of the pulmonary tissue, such as is often present in Bright's disease, also modifies the physical conditions produced by the pneumonic process. Not only are these secondary pneumonias often characterized by the exuded liquids being less coagulable than are those resulting from primary inflammations, but the emigration of leucocytes is usually less abundant, and the proliferation of the alveolar endothelium appears to constitute a somewhat more prominent part of the process, so that a greater proportion of large nucleated cell-forms are found within the pulmonary alveoli.

The pneumonic process may terminate in the four following ways:—

1st. *In Resolution.*—The gradual return of the lung to its normal condition is much the more frequent termination of croupous pneumonia. The coagulated materials liquefy, the young cells entangled in them undergo complete fatty degeneration and disintegration, and thus the inflammatory products become so altered that they can be removed by absorption. Granular pigment is also mixed with the softened matters and appears in the expectoration. This is probably partly derived from the extravasated blood, and is partly that which normally exists in the interlobular connective tissue. Where this process of liquefaction and disintegration is taking place in the lung, the granular appearance of its cut surface is completely lost. It is of a yellowish-grey colour, and a tenacious puriform liquid can be expressed from its substance. As the softened matters become absorbed, the circulation is gradually restored, and the organ ultimately attains its normal characters.

2nd. *In Abscess.*—The formation of an abscess is a very rare result of simple pneumonia. It may, however, take place if the emigration of blood-corpuscles is very abundant and the cell-proliferation is very active. The pus is always mixed with broken-down pulmonary tissue. When pneumonic processes are induced by septic matters and are thus disseminated, as in pyæmia, the formation of abscess usually occurs. (See "Pyæmia.")

3rd. *In Gangrene.*—Still more rare than the preceding is the occurrence of gangrene. Two conditions appear to be principally concerned in bringing about this result:—one is the interference with the supply of blood by the extensive formation of coagula in the pulmonary and bronchial vessels, together with considerable hæmorrhage into the pulmonary tissue; the other, is the contact of putrid substances with the pneumonic tissue,—as the putrid secretion in a dilated bronchus.

4th. *In Chronic Pneumonia and Phthisis.*—If the inflammatory process does not subside and the exuded substances are not absorbed, the alveolar walls gradually become involved. These become thickened by a new growth of fibro-nucleated tissue, and thus is produced more or less fibroid induration of the organ. (See "Interstitial Pneumonia.") This termination of croupous pneumonia is comparatively rare. In very exceptional cases the continuance of the inflammatory process leads to the softening and destruction of the alveolar walls, and disintegration and excavation of the lung is the ultimate result.

CATARRHAL PNEUMONIA.

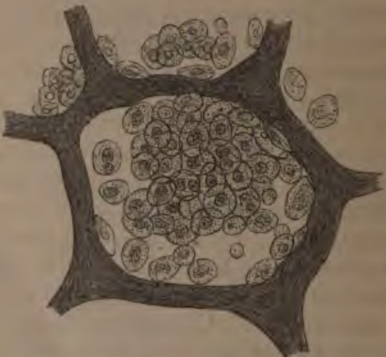
Catarrhal, lobular, or *broncho*-pneumonia differs from the preceding, inasmuch as in it there is but little or no exudation of coagulable material, the process being mainly characterized by proliferation of the alveolar endothelium. It thus somewhat resembles catarrhal inflammation of mucous membranes—hence the term "catarrhal" which is applied to it. This form of pneumonia is almost invariably at its commencement limited to single lobules or to groups of lobules, and does not like the croupous variety involve simultaneously large tracts of pulmonary substance. It is consequently also known as *lobular* pneumonia.

Catarrhal pneumonia very rarely occurs as an independent affection, but is very constantly preceded by catarrhal changes in the bronchial mucous membrane. The catarrhal process appears very frequently to be a direct extension of the inflammation from the smaller bronchi to the air-vesicles. In other cases it is determined by pulmonary collapse. Collapse of the air-vesicles—whether it be due to bronchial obstruction or to diminished inspiratory power—especially favours the occurrence of this catarrhal change, as is evidenced by the frequency with which the latter is entirely limited to the collapsed portions of the lung. The occurrence of collapse is followed by congestion and œdema of the collapsed portions of the pulmonary tissue, and it is this local congestion which appears to determine the catarrhal process. Catarrhal pneumonia presents acute and chronic varieties.

ACUTE CATARRHAL PNEUMONIA.—Acute catarrhal pneumonia is most common in children and young adults. In children it is more common than the croupous variety. It is usually preceded by capillary bronchitis, and is an especially frequent complication of measles and hooping-cough.

The process comprises more or less hyperæmia and serous exudation from the alveolar blood-vessels, together with enlargement and proliferation of the alveolar endothelium. There appears to be no exudation of coagulable material such as occurs in croupous inflammation, and although a few leucocytes may escape from the hyperæmic vessels, there is no abundant emigration. The newly formed elements are large and spheroidal, usually con-

FIG. 81.



Catarrhal Pneumonia. Showing the large epithelial-like cells which fill the alveolar cavity. These are already commencing to undergo fatty changes. × 200.

taining one, sometimes two or three, bright nuclei, and in a more advanced stage, molecular fat. As they increase in number, they completely fill the alveolar cavity. (Fig. 81.) On section of the lung, the pneumonic lobules are seen scattered through its substance, as small, reddish grey, ill-defined nodules, with a smooth and slightly granular surface. The immediately surrounding lung tissue is usually hyperæmic and œdematous, and frequently collapsed. In a more advanced stage the newly formed elements undergo fatty metamorphosis, and the nodules change from a reddish-grey to a yellowish-white colour. In addition to these pneumonic nodules, there are frequently seen minute spots of a more decidedly yellow colour. These, which are very common in capillary bronchitis, are merely alveoli containing mucus and purulent matter which has been drawn in by the act of inspiration. They may exist quite independently of any inflammatory change, and must not be confounded with the pneumonic nodules. As the process continues, the numerous small pneumonic patches may gradually coalesce, and thus there may be formed larger tracts of greyish consolidation. Resolution and the return of the lung to its normal condition may occur in this stage. Such a result, however, partly owing to the abundant growth of large cells, is less common than in croupous pneumonia. Very frequently the fatty metamorphosis of the new elements is incomplete, they do not become absorbed, but the pneumonic masses become caseous, and the disease thus passes into the chronic stage.

Chronic Catarrhal Pneumonia.—Chronic catarrhal pneumonia may be the result of the above-described acute process, or it may be from the commencement a chronic change. The process, like the acute, is very constantly preceded by catarrh of the bronchial mucous *membrane,* and it is characterized mainly by the development and accumulation of large cellular elements within the pulmonary alveoli and terminal bronchioles. The pneumonic nodules, however, very rarely undergo complete fatty metamorphosis and resolution, but gradually become caseous, and the resulting caseous masses become themselves the seat of subsequent changes, whilst at the same time they cause changes in the pulmonary tissue. As this form of pneumonia plays so prominent a part in pulmonary phthisis, it will be treated of in the chapter devoted to the consideration of this disease. (See "Pulmonary Phthisis.") It will be sufficient in the present place to state, that when a catarrhal pneumonic process becomes chronic, it in all cases leads to changes in the alveolar walls—changes which are characterized by the development in them of a fibro-nucleated lymphoid tissue.

INTERSTITIAL PNEUMONIA.

Interstitial or chronic pneumonia is a chronic inflammatory process in the lungs which leads to a fibroid induration of the pulmonary texture—an induration which is due to a thickening of the alveolar walls and of the interlobular tissue by a fibro-nucleated growth, and to the gradual obliteration by this growth of the alveolar cavities. It may be stated generally, that all chronic inflammatory processes in the lungs are attended by more or less fibroid induration of the organs, and in this respect, therefore, these processes resemble similar ones in other parts—*e. g.*, in the liver, kidney, and mucous membranes. In chronic phthisis, for example, as will be seen hereafter, a fibroid change plays a very prominent part, and in the most chronic cases the pulmonary tissue may be almost completely replaced by a dense fibroid growth. Croupous pneumonia, as has been already stated, may pass into a *chronic* condition, in which case it leads to a fibroid *thickening* of the alveolar walls, and consequently to more or less induration of the pulmonary texture. Catarrhal pneumonia, again, which has a greater tendency to become chronic than the exudative process, may lead to considerable pulmonary induration:—this will also be alluded to when treating of pulmonary phthisis. Lastly, the thickening of the peri-bronchial tissue which sometimes occurs in chronic bronchitis, may gradually extend and involve the alveolar walls so as ultimately to produce extensive obliteration of the pulmonary alveoli.* In all these cases the fibroid change is an evidence of the chronicity of the inflammatory process.

Although fibroid changes in the lungs may thus owe their origin to these various chronic inflammatory processes, it is only in those cases in which inflammation leads to those pulmonary lesions included under the common term of "phthisis," that they constitute a frequent form of pulmonary affection. Indeed, independently of phthisis, they are amongst the rarest forms of pulmonary disease; and it is to these exceptional cases that the application of the term "interstitial" or "chronic pneumonia" is commonly restricted.

Interstitial pneumonia, in this restricted sense, is the disease which received from Sir D. Corrigan the name of "cirrhosis." It is commonly unilateral; and is characterized by a very extensive fibroid induration and consequent contraction of the organ, by obliteration of the alveolar cavities, more or less pigmentation, and usually by dilatation of the bronchi. The appearance presented by the lung in these cases is very characteristic. It is diminished in size; the tissue is smooth, dense, firm,—in parts almost cartilaginous in consistence; and it is irregularly mottled with black pigment. The alveolar structure of the lung is in most parts completely destroyed, and on section the dilated bronchi are often seen as numerous large openings scattered over its surface. The dilated bronchi frequently become the seats of secondary inflammatory processes, which may lead to ulceration and ultimately to extensive excavation of the indurated tissue; but there is a complete absence of any of those caseous changes which are so characteristic of ordinary phthisis. The pleura is almost invariably considerably thickened and adherent.

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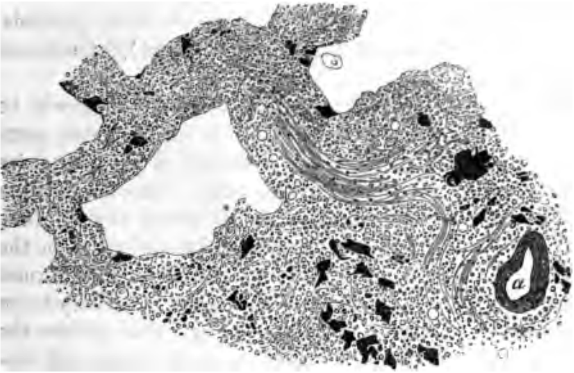
* See case by the Author—"Interstitial Pneumonia," Trans. Path. *Soc. Lond., 1872.*

When the lung is examined microscopically, it will be found that the alveolar structure has been in most parts completely replaced by a fibro-nucleated or by a more densely fibroid growth, presenting the characters already described as those met with in cicatricial tissue. (See Fig. 63.) The new growth may commence either in the alveolar walls or in the interlobular tissue. The former appears to be usually the case when it is secondary to an exudative or catarrhal pneumonic process. Where the change is not far advanced and the alveoli are still distinct, their walls will be seen to be thickened by a fibro-nucleated growth, and their cavities sometimes to be filled with large epithelial-like cells, or less frequently, with leucocytes. (Fig. 82.) The characters of the new growth in the alveolar walls and in the interlobular tissue present certain variations. In the earlier stages of the inflammatory process it consists principally of small spheroidal elements which are often grouped within the meshes of delicately fibrillated reticulum; but when more advanced the fibrillation is much more marked, and associated with the small spheroidal elements there are frequently some elongated fusiform cells such as are so often found in embryonic tissue which is in the process of forming a fibrous structure.

With regard to the etiology of interstitial pneumonia—it probably, as already stated, almost invariably owes its origin to some antecedent more acute pneumonic process of either the exudative or catarrhal type, or to bronchitis. It is maintained, however, by many pathologists that a fibroid change may occur in the lungs as a primary and independent affection, and that consequently interstitial pneumonia occupies the same pathological position as indurative processes in the liver and kidneys. That such a view is correct appears to the author to be extremely doubtful.

FIG. 82.



Interstitial Pneumonia. From a case of so-called "cirrhosis" of the lung, in which the disease was unilateral. The bronchi were much dilated, and there was a complete absence of any caseous change. The drawing shows the new fibro-nucleated growth, both in the alveolar walls and in the interlobular tissue, also the pigmentation. At *a* a divided bronchus is seen. × 100.*

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* When this specimen is examined with a higher magnifying power, a delicate reticulum can be seen between the cellular elements, similar to that represented in Fig. 48, but less marked.

CHAPTER XXXVIII.

PULMONARY PHTHISIS.

By pulmonary phthisis is understood a disease of the lungs which is characterized by progressive consolidation of the pulmonary texture, and by the subsequent softening and disintegration of the consolidated tissue. Respecting the nature of the morbid processes which lead to this disintegration of the lungs—various opinions have from time to time been held by pathologists, and this diversity of opinion exists to some extent even at the present day. According to the older views, which were based upon the teaching of Laennec, phthisis was regarded in all cases as a *tuberculous* disease, tubercle was looked upon as a specific non-inflammatory growth which was characterized by the caseous degeneration which it invariably underwent (see "Acute Tuberculosis"), and this caseous metamorphosis was held to be such a distinguishing peculiarity of the growth that all caseous masses came to be regarded as tuberculous, and phthisis, in which caseation plays such a prominent part, was consequently regarded as a tuberculous disease. The various consolidations of the pulmonary tissue were described as "infiltrated tubercle," and tubercle in some form or other was regarded as so essential a constituent of the disease, that "phthisis" and "pulmonary tuberculosis" came to be quite synonymous terms.

These older views respecting the nature of phthisis have undergone various modifications during recent years. When the application of the term "tubercle" became limited by Virchow and his followers to the grey granulation, it was evident that such views were no longer tenable, and at the present time many, in accordance with the advocacy of the late Professor Niemeyer, regard tubercle as only an occasional element in the causation of the disease. In considering how far tubercle plays a part in the production of phthisis, it must be borne in mind that this growth is now known to be an inflammatory one. The miliary lesions which are commonly known as tubercular, are merely the anatomical results of chronic inflammatory processes limited to minute circumscribed areas in tissues which either belong or have a close relation to the lymphatic system; and although they consist in the main of a small-celled lymphoid tissue, they present certain differences in their anatomical characters according to the structure of the organ in which they originate. (See "Acute Tuberculosis.") In the lungs it has been seen that they consist not only of that lymphoid tissue which is so characteristic of tubercular lesions, but also of accumulations of epithelial-like cells within the pulmonary alveoli; and further, that whereas this lymphoid tissue very frequently becomes developed into a fibrillated structure, the epithelial-like elements invariably undergo retrogressive metamorphosis. (See "Tuberculosis of the Lungs.")

The prominent place which the production of a lymphoid tissue plays in these chronic inflammatory processes in the lungs, is probably to be explained by the anatomical peculiarities of the pulmonary texture. This lymphoid tissue is not only largely met with in the neighbourhood of the minute bronchioles, but the recent investigations of Buhl and others, already alluded to, would seem to show that the alveolar walls are intimately *connected with the* lymphatic capillaries, and that the large cells lining them correspond with the lymphatic endothelium.

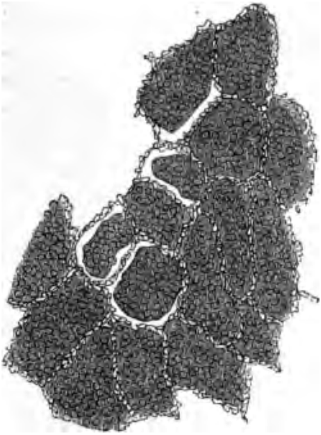
The anatomical changes in the lungs which occur in pulmonary phthisis are precisely analogous to those which are met with in acute tuberculosis. They differ mainly in this respect—that whilst in the latter disease these changes are usually limited to minute areas (hence the miliary character of the lesions), in the former they commonly involve much wider tracts of tissue.

In studying pulmonary phthisis, it will be advisable in the first place to describe the various structural changes which are met with in the lungs, together with the more important alterations which they produce in the physical characters of the organs; and subsequently to examine into the nature of the morbid processes upon which these changes depend, and to draw some general conclusions respecting the pathology of the disease.

The structural changes met with in the lungs in phthisis are mainly of three kinds:—1st. *An accumulation of large epithelial-like cells within the pulmonary alveoli;* 2nd, *a thickening of the alveolar walls by a small-celled lymphoid tissue, together with, in most cases, the growth of a similar tissue around the minute bronchioles;* and 3rd, *an increase in the interlobular connective tissue.* These three kinds of morbid change are almost invariably associated with one another, although in very different degrees. The preponderance of one or other of them produces those variations in the physical characters of the lungs which are met with in the different stages, and in the different varieties of the disease. In addition to these more common changes, a fibrinous exudation enclosing leucocytes, such as is found in croupous pneumonia, is sometimes met with in phthisical lungs. These several structural changes must now be considered separately.

1st. *An accumulation of large epithelial-like cells within the pulmonary* alveoli is one of the most frequent changes met with in phthisis, and this change is precisely similar to that already described as occurring in catarrhal pneumonia. The alveoli are found filled with large nucleated elements which are the offspring of the cells normally lining the alveolar walls—cells the endothelial nature of which has been already alluded to. (See Fig. 81.) In some cases this alveolar accumulation may constitute almost the only morbid change, and although the alveolar walls may be found slightly thickened here and there by a small-celled lymphoid tissue, the great bulk of the pulmonary consolidation is due to the stuffing of the alveolar cavities with catarrhal products. (Fig. 83.)

FIG. 83.



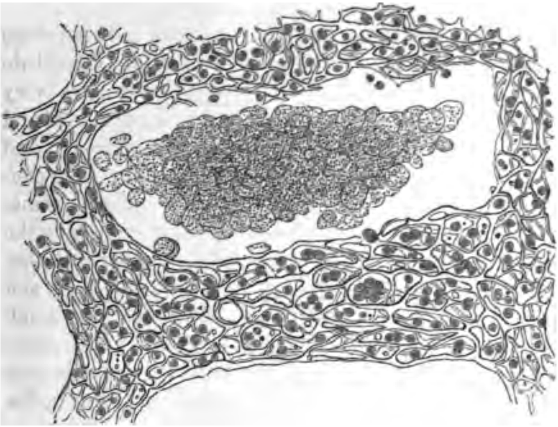
Section of Lung from a case of very Acute Phthisis. Showing the accumulations of large cells within the alveoli. The alveolar walls are almost completely free from any small-celled growth. In some parts a free space is seen between the alveolar walls and their contents: this is simply due to the shrinking of the latter caused by the hardening of the specimen. × 50. (Compare with Fig. 58.)

In some parts—those in which the change is the most recent—the large cells which fill the alveoli and the alveolar walls will be found but little altered, but in the greater portion of the consolidated tissue the cells will be seen in various stages of retrogressive metamorphosis, and the alveolar walls destroyed; whilst in those tracts of tissue in which the process is most advanced all trace of structure is lost, and nothing is seen but a granular débris. These changes are precisely analogous to those met with in many of the larger nodular lesions of acute tuberculosis. (See Figs. 57 and 58.)

The appearances presented by the lungs in those cases in which the structural changes above described constitute almost the only cause of the consolidation, are very characteristic. The consolidated tissue is quite soft and friable, breaking down very readily under the finger, and there is a complete absence of any induration. The consolidation, although frequently almost uniform, sometimes presents a somewhat lobulated outline, indicating the implication of different groups of the pulmonary lobules. The colour varies from a reddish to a yellowish-grey, and scattered through the consolidated mass are often small portions of a more decidedly yellow tint. These latter correspond with those parts in which the retrogressive changes are the most advanced, and they are even softer in consistence than the surrounding tissue. In many parts the consolidated tissue will be found broken down, so as to form cavities of various sizes. These always possess irregular walls, which are quite soft and friable like the solid tissue which surrounds them.

2nd. *A thickening of the alveolar walls by a small-celled lymphoid tissue, together with, in most cases, the growth of a similar tissue around the terminal bronchioles,* is very constantly associated with the former intra-alveolar change. The characters of this new tissue present every variation from a growth composed almost entirely of small spheroidal elements resembling lymph-corpuscles, such as is represented in Fig. 56, *a*, to one in which these elements are grouped within the meshes of a more or less densely fibrillated network, as seen in Figs. 48, 56, *b*, and 63, *a*, and these variations correspond with differences in the stage of the new growth and in the rapidity of its development. In many parts the alveolar cavities may be found completely obliterated and replaced

FIG. 84.



Section of Lung from a case of somewhat Chronic Phthisis. Showing the thickening of the alveolar walls by a small-celled lymphoid tissue which is becoming fibroid, together with an accumulation of large cells within the alveolar cavity which are undergoing retrogressive changes. × 200.

by this new tissue, whilst in others, where the change is less advanced, their walls will be seen to be more or less thickened by it, and their cavities to be filled with partially or completely degenerated epithelial-like elements. (Fig. 84.) Although from the fibrillation of the inter-cellular network the new growth appears in many places to be undergoing a process of progressive development, in others it is equally evident that it is undergoing retrogressive changes, and the granular débris into which it has become converted is often seen associated with the degenerated epithelial-like elements, the two together producing tracts of softened, yellowish, caseous material.

Respecting the alteration which the growth of this small-celled tissue produces in the physical characters of the lungs—it may be stated generally, that it usually leads to more or less induration of the pulmonary texture. The extent of this induration, however, will vary with that of the fibrillation of the new tissue. If the tissue be almost entirely cellular, such as is the case when it is very rapidly developed, it will produce but little if any induration of the pulmonary consolidation, which, consisting mainly of the alveolar catarrhal products, will be soft and friable in consistence, much resembling that which has been already described. When, on the other hand, as is more frequently the case, there is any marked fibrillation of the new growth, there will be a corresponding induration of the consolidated tissue. In many cases these changes produce uniform tracts of indurated consolidation of a greyish colour mottled with black pigment, in which there may be scattered here and there yellowish patches corresponding with those portions which have undergone retrogressive fatty changes.

3rd. The remaining structural change which is met with to a greater or less extent in most cases of pulmonary phthisis, consists in *an increase in the interlobular connective tissue.* This tissue, which surrounds the bronchi and blood-vessels and contributes to the formation of the alveoli, is found not only increased in amount but also altered in character. It is usually richly cellular, and in the various stages of its growth it presents all the variations met with in connective tissue which is the seat of a chronic inflammatory process. (See Figs. 63 and 82.) It frequently exhibits, in some parts, a distinctly reticulated structure precisely similar to that of the lymphoid growth in the alveolar walls (see Fig. 84), but it has a much greater tendency to form a dense fibroid tissue than has the alveolar growth. In the most chronic cases of phthisis this interlobular growth may constitute the predominant structural change, and large tracts of the pulmonary texture may be found completely replaced by it. (See "Interstitial Pneumonia.")

An increase in the interlobular connective tissue in phthisis—inasmuch as the new tissue has so marked a tendency to become dense and fibroid—leads to extensive induration of the pulmonary texture; and further, owing to the contraction which the tissue tends to undergo, its growth ultimately produces a corresponding contraction of the diseased lung. In all those cases of phthisis in which there is either a thickening of the alveolar walls or an increase in the interlobular connective tissue, any cavities which may exist in the consolidated and indurated tissue are characterized by the tough and fibroid character of their walls, these presenting a marked contrast to the soft friable tissue which surrounds the cavities in those cases in which the pulmonary consolidation is mainly due to a catarrhal intra-alveolar growth.

4th. The presence of a fibrinous exudation and leucocytes within the pulmonary alveoli is only occasionally met with in phthisis. It may, however, be found in lungs which have previously undergone some of the structural changes already described. It is perhaps most common as an acute affection occurring at the base of a lung, the apex of which is already the seat of more chronic disease. It must also be borne in mind that an exudative inflammatory process may, in very exceptional cases, terminate in phthisis. (See "Croupous Pneumonia.")

These various changes may involve wide tracts of the pulmonary tissue, or they may be limited to small circumscribed areas. The causes of these differences in their distribution will be seen when considering the nature and etiology of the morbid processes to the existence of which they owe their origin.

PATHOLOGY.—Having thus briefly described the various structural changes met with in the lungs in phthisis, it remains to consider the nature of the morbid processes upon which they depend. In the first place it is evident that these changes are analogous to those which have been seen to occur in the several forms of pulmonary inflammation, especially in catarrhal and interstitial pneumonia. The accumulation of epithelial-like cells within the alveoli in catarrhal pneumonia, with, in the more chronic cases, the ultimate thickening of the alveolar walls; and the increase in the interlobular connective tissue which characterizes the interstitial process, closely resemble the phthisical lesions. These considerations, together with those derived from the study of the etiology of the disease, are sufficient to justify the conclusion that the morbid processes which lead to the consolidation and subsequent disintegration of the lung come within the category of *inflammation,* and that the differences in the anatomical changes to which they give rise are due to differences in the intensity, in the duration, and in the mode of origin of the inflammatory process.

In considering the causes of these differences in the anatomical changes in the lungs, it is important to bear in mind what has been already stated respecting the variations in the character of the textural alterations in inflammation which are produced by differences in the intensity and duration of the inflammatory process. (See "Varieties of Inflammation.") When studying the process of inflammation, it was seen that the less severe and more prolonged the process the greater was the tendency of the resulting textural changes to be limited to the elements immediately adjacent to the blood-vessels and lymphatics, whereas in inflammations of somewhat greater intensity more distant elements became involved. Further, that whereas in the former case these changes usually resulted in the formation of a small-celled tissue which tended to become fibrous, in the latter, the more distant elements—being in most cases incapable of further development—tended to undergo retrogressive changes. In the lungs, the truth of these propositions was borne out by the differences which were seen to exist in the anatomical characters of the lesions in acute tuberculosis. In this infective process it appeared to be probable that the more severe the irritation of the infective particles the more liable were they to cause a proliferation of the large epithelial-like cells contained within the alveoli, which cells being apparently incapable of further development underwent retrogressive changes; whereas when the irritation was less severe, its influence tended to be limited to the elements in the alveolar walls and interlobular tissue, and the development of a small-celled lymphoid structure which tended to become fibroid was consequently the result. (See "Tuberculosis of the Lungs.")

If the pathology of these inflammatory processes in the lungs be kept in view, the explanation of the differences in the anatomical characters of the lesions in pulmonary phthisis becomes tolerably evident. In those cases in which the inflammatory processes are of slight intensity and of long duration, the most marked structural change will consist in the development of a small-celled growth in the alveolar walls and in the interlobular tissue—a growth which tends to become developed into a fibroid structure; whereas in those cases in which the inflammation is of greater intensity a proliferation of the large nucleated elements contained within the alveoli will constitute the more prominent part of the process.

The intensity of the inflammatory process not only determines to a great extent the anatomical characters of the pulmonary consolidation, but also the subsequent changes which take place in the newly formed elements. These changes tend towards death or progressive development. The latter, however, can only take place in the small-celled tissue which is produced in the alveolar walls and interlobular structures; the epithelial-like elements, being probably incapable of further organization, quickly undergo retrogressive metamorphosis. In those cases in which the intensity of the process is considerable, not only do the epithelial-like cells which have accumulated within the alveoli quickly degenerate and break down, but any small-celled tissue which may have been developed in the alveolar walls or around the terminal bronchioles also softens and dies, and thus the vitality of large tracts of the pulmonary consolidation may become destroyed.

In explaining this death and disintegration of the pulmonary consolidation which constitutes so essential a feature of the disease, it must be borne in mind that although this may be partly due to the direct destruction of vitality from the intensity of the inflammation, the nutrition of those newly formed elements which have accumulated within the alveolar cavities also becomes impaired owing to the interference with the circulation which results from the pressure which they exercise upon the capillaries in the alveolar walls, and from the new growth of tissue which takes place around these vessels. It is this interference with the circulation in the walls of the alveoli which not only aids in the destruction, but also prevents that absorption of the inflammatory products which so often occurs in simple acute catarrhal pneumonia.

In those cases of phthisis, on the other hand, in which the inflammatory process is less severe, the small-celled tissue developed in the alveolar walls and around the terminal bronchioles tends to become developed into a more or less completely fibrillated structure, and the more chronic the course of the disease the greater is this tendency.. The new growth in the interlobular tissue, inasmuch as it is usually only met with in the more chronic forms of the disease, almost invariably becomes indurated and fibrous. It is these two kinds of change in the newly formed elements, the one tending towards death and the other towards progressive development, which produce the caseation and softening on the one hand, and the induration on the other, which associated in . such various degrees, make up the diverse physical characters of the phthisical lung.

In studying the etiology of the inflammatory processes which give rise to pulmonary phthisis, it becomes evident that three different agencies are concerned. These are, *direct irritation*, *infection*, and *predisposition*.

The *direct irritation* of the lungs through the medium of the bronchi is undoubtedly the most important agent in the production of phthisis. The bronchial mucous membrane, communicating as it does with the external air, is especially liable to injury, and the extreme frequency with which the development of phthisis is preceded by successive attacks of bronchial catarrh is a well-established clinical fact, the important bearing of which upon the successful treatment of the disease it would be difficult to over-estimate. That catarrhal processes in the smaller bronchi are often followed or accompanied by inflammatory changes in the pulmonary alveoli was seen when studying the pathology of catarrhal pneumonia. In explaining these changes, however, it must be borne in mind that although the thickening of the alveolar walls is in part the result of the primary irritation, the presence of the degenerated catarrhal products within the alveolar cavities must also produce an injurious effect, and so may *be an additional* cause of the alveolar growth. These catarrhal processes in the bronchi which are such frequent precursors of the pulmonary consolidation, also give rise to a gradual thickening of the bronchial mucous membrane, to an increase in the peribronchial connective tissue, and often to more or less ulceration and irregular contraction and dilatation of the tubes.

Another agency in the production of phthisis is *infection*. This infection is precisely similar to that which has been already described as causing general tuberculosis. By it is understood the property possessed by certain chronic inflammatory products—especially by those which have become caseous—of inducing secondary inflammatory processes in other parts. Limited tuberculosis differs from the general disease only in the extent to which the infective materials are distributed. Whereas in the general affection the dissemination of the infective substances takes place principally by means of the blood-vessels, in the more limited processes the dissemination is effected by means of the lymphatic vessels or serous canals. In the lungs, limited infective processes are exceedingly common in phthisis, and they give rise to many of the miliary nodules of induration which are so frequently met with in phthisical lungs. The source of infection in these cases is usually some caseous induration already existing in the lung, so that the infective process usually supervenes upon pre-existing phthisis.

The remaining agency, which plays a very important part in a large proportion of the cases of phthisis, is *predisposition*. This predisposition appears to consist mainly in an abnormal susceptibility of the broncho-pulmonary tissues to the various kinds of injurious irritation.

In conclusion, allusion must be made to the different varieties of pulmonary phthisis. Although the variations observed in the physical characters of phthisical lungs and also in the clinical history of the disease, have led to its subdivision into different kinds, it appears to the author that there are no pathological grounds for any such subdivision. The variations in the anatomical characters of the lungs depend principally upon variations in the intensity and duration of the inflammatory processes which give rise to the pulmonary consolidation, and also upon the parts which primary irritation and infection play respectively in the causation of the disease.

CHAPTER XXXIX.

CHANGES IN THE BLOOD AND CIRCULATION.

HYPERÆMIA.

HYPERÆMIA or congestion is excess of blood in the more or less dilated vessels of a part. Whatever increases the pressure of the blood, or diminishes the resistance of the vessels, may be a cause of hyperæmia. Hyperæmia is *active* or *arterial*, and *mechanical* or *venous*. These two varieties must be considered separately.

ACTIVE HYPERÆMIA.

Active hyperæmia is an excess of blood in the arteries of a part, with, in most cases, an acceleration of the flow.

CAUSES.—The causes of active hyperæmia may be divided into those which increase blood-pressure, and those which diminish arterial resistance.

1. *Increased Blood-pressure.*—This occurs most commonly from interruption of the main current of blood in any particular part, owing to which increased pressure is thrown upon the collateral vessels. These vessels thus become dilated, the amount of blood in them is increased, and the flow is accelerated. This, which is known as *collateral hyperæmia,* is seen after the obstruction of the main current from any cause, as from the ligature of the vessel, or from its occlusion by a thrombus or embolus (see "Embolism").

General obstruction in the capillaries of a part will in the same way cause a compensatory hyperæmia. This is exemplified by the application of external cold causing contraction of the superficial capillaries and congestion of internal organs; and by obstruction of the capillaries in one part of an organ causing hyperæmia of the parts adjacent.

2. *Diminished Arterial Resistance.*—This is much the most frequent cause of active hyperæmia. It may arise from—

a. Relaxation or paralysis of the wall of the vessel.—The relaxation of the muscular coat of an artery and the consequent dilatation of the vessel, may be owing either to the direct paralysis of the vaso-motor nerve supplying it, or to the irritation of a sensory nerve. The effects of direct paralysis of the vaso-motor nerves are seen in the active congestion of the head and neck which follows pressure upon the sympathetic in the neck, as by an aneurism; and in the unilateral congestion which results from experimental sections or disease of one-half of the spinal cord. Some emotional conditions also are attended by paralysis of the vascular nerves and consequently by active hyperæmia: this is seen in blushing. Certain substances again taken internally produce vaso-motor paralysis, as the nitrite of amyl, alcohol, tobacco, &c.

Relaxation and dilatation of the arteries is also produced by the irritation of a sensory nerve, in those parts in which the nerve orginates. Active hyperæmia from this cause has already been described when speaking of it as the earliest change in the process of inflammation. The irritation received by the sensory nerves is reflected by the vaso-motor centre to the blood-vessels, and causes dilatation of the vessels and increased rapidity of flow. In inflammation, this irritation is so severe as to cause not only dilatation of the vessel, but also changes in its walls, which ultimately lead to the retardation of the blood-flow and to exudation of liquor sanguinis and blood-corpuscles. If the irritation be less intense or less prolonged in its action it produces simply dilatation of the vessels and increased rapidity of flow — *i.e.*, active hyperæmia. This is seen in the congestion of the skin which results from friction, heat, and many irritating substances; in the priapism that sometimes results from the passage of a catheter; and in many similar conditions.

β. Sudden removal of external pressure.—The sudden removal of external pressure from vessels is followed by their dilatation, and consequently by hyperæmia. As examples of hyperæmia from this cause may be mentioned that which results from dry cupping, and from the sudden removal of ascitic fluid, and of the fluid from a hydrocele.

γ. Atony of the walls of the vessels from mal-nutrition.—This is a much less important cause of hyperæmia. Fatty degeneration of the muscular and internal coats of the smaller arteries may, however, in some cases, lead to their dilatation, and thus be a cause of active hyperæmia.

Results.—The results of active hyperæmia are principally such as might be expected to follow from an increase in the amount of the arterial blood, and in the rapidity of its flow, in any particular organ or tissue. There is increased redness and pulsation, a sensation of throbbing being often experienced by the patient. There is also an increase in bulk. The temperature at the same time undergoes a marked elevation; as much as 10° Fahr. has been observed after injuries of the spine, and experimental sections of the sympathetic. Serous effusions, hæmorrhage, and thrombosis—so common as results of mechanical hyperæmia—are rarely met with. If the hyperæmia be of long duration, the small arteries become permanently enlarged, and their walls thickened. Function may, or may not, be interfered with. It is in the nervous centres that functional changes are most frequently met with. They include great excitability, paræsthesiæ of sight and hearing, convulsions, &c.

MECHANICAL HYPERÆMIA.

In mechanical hyperæmia, the excess of blood is principally in the veins, and the flow, instead of being accelerated, is retarded.

Causes.—The causes of mechanical hyperæmia are such as interfere with the return of the blood by the veins, either by directly impeding its exit from any vein or system of veins, or by diminishing the normal circulating forces. They are—

1. *A direct Impediment to the Return of Blood by the Veins.*—This is the most fertile cause of mechanical hyperæmia. Any obstruction to the return of blood by the veins is followed by distension and impeded flow behind the obstruction. The congestion of some of the abdominal viscera which results from the obstruction to the portal circulation in cirrhosis of the liver; that of the lung in mitral constriction and regurgitation; that of the systemic circulation in insufficiency of the tricuspid valve; and that of the lower extremities from the pressure of the gravid uterus on the iliac veins, are a few of the numerous familiar examples of mechanical hyperæmia from this cause.

2. *Gravitation.*—This becomes an important auxiliary in the production of hyperæmia in disease, especially when it is associated with diminished cardiac power. The effect of gravitation in determining congestion of the most dependent parts is exemplified in chronic exhaustive and in many of the acute febrile diseases, in which the nutrition generally becomes impaired, the heart's power weakened, and in which the patient is unable frequently to change his position. The integuments of the back, and

the posterior portions of the lungs, are the parts which are thus most frequently affected.

3. *Increased Local Resistance.*—This results from diseased conditions of the arterial walls, owing to which they either lose their elasticity and contractility and thus their power of equalizing and regulating the blood-flow, or become considerably enlarged. In either case the circulation will be impeded, and accumulation of blood and retardation of flow take place in the veins beyond. Such conditions arise from atheromatous, fatty, and calcareous changes in the arterial walls, and are most common in advanced life. The part they play in the production of senile gangrene has been already alluded to (see " Senile Gangrene").

4. *Diminished Cardiac Power.*—This is one of the most important causes of mechanical hyperæmia, especially when it is associated with any of the preceding ones. The motor power of the heart becomes impaired in many of the chronic exhausting diseases, also in the acute febrile diseases, as in typhus and typhoid fever, and in all those conditions of degeneration and softening of its structure which lead to the dilatation of its cavities. In whichever of these ways the *vis a tergo* is diminished it will tend to produce venous hyperæmia.

RESULTS.—Long continued mechanical hyperæmia leads to impairment of vitality and function. The tissues gradually atrophy and undergo retrogressive changes, although from the amount of serosity and blood which they contain their size and absolute weight may be increased. Their temperature becomes lowered. The most important results, however, of this variety of hyperæmia are *fibroid induration, transudation of serum, hæmorrhage, thrombosis,* and *gangrene.*

1. *Fibroid Induration.*—This, which is due to a gradual increase in the connective tissue around the blood-vessels, is one of the most important results of long continued

mechanical hyperæmia. The interstitial growth leads to atrophy of the other structures, and thus to impairment of the functions of the organ. In the stomach, it produces atrophy of the glandular structures; in the kidney, compression of the urine-tubes; in the liver, obstruction to the portal circulation; in the heart, diminution in motor power. The alterations which this change produces in the physical characters of the organs—viz., a hardness and induration associated with abnormal redness or pigmentation due to the excess of blood, are exceedingly characteristic.

2. *Transudation of Serum.*—This gives rise to œdema and dropsical effusions. Its occurrence is greatly favoured by the stretching of the walls of the vessels, and by the damage which their structure sustains. The transuded serum usually differs from blood-serum in being of lower specific gravity, and in containing more water and less of the solid constituents. The greater the pressure, the more nearly does the transuded liquid resemble the liquor sanguinis, and the greater is the amount of albumen which it contains. If the pressure be very great it may yield a fibrinous coagulum.

3. *Hæmorrhage.*—This is another result of mechanical hyperæmia. It usually occurs only when the obstruction to the venous current is very great. Those vessels which are the least supported are the first to give way. The hæmorrhage into the stomach in cirrhosis of the liver, and into the lung in mitral disease, are familiar examples of hæmorrhage from this cause.

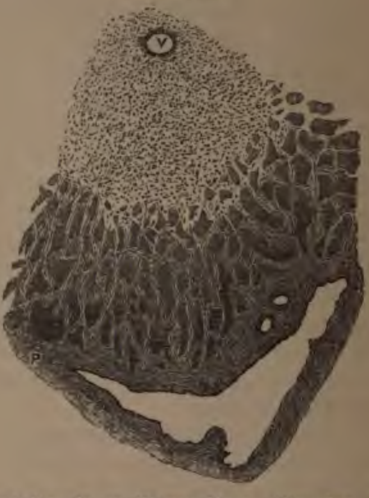
Not only does blood escape from the vessels by rupture of their walls in mechanical hyperæmia, but the red blood-corpuscles pass through the walls of the capillaries into the surrounding tissues without rupture taking place. This passage of the red corpuscles through the capillary walls, which was discovered by Cohnheim, may be observed in the web of the frog's foot after ligature of the femoral vein. The corpuscles in passing through the vessel become constricted in their centre, so as to assume an hour-glass shape. This emigration only occurs when the obstruction is considerable.

4. *Thrombosis.*—This, as a result of mechanical obstruction, will be described in the following chapter.

5. *Gangrene.*—This only occurs from mechanical hyperæmia when the obstruction is very general and complete. It has been already described under the head of "Gangrene."

MECHANICAL HYPERÆMIA OF THE LIVER.—Long continued mechanical hyperæmia of the liver gives rise to the

FIG. 85.



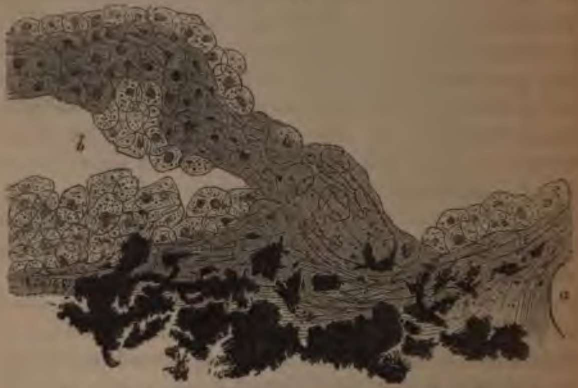
Red Atrophy, or Nutmeg Liver. Showing the destruction of the liver-cells and the pigmentation in the central portions of the acinus, together with the new growth of connective tissue at the periphery. V. Hepatic vein. P. Portal canal. × 50.

condition known as *Red Atrophy* or *Nutmeg Liver*. This is the condition which so frequently results from disease of the heart. The change is characterized by a large accumulation of blood in the hepatic veins, by dilatation and thickening of these veins, by atrophy of the hepatic cells in the central portions of the acini, and by an increase in the interlobular connective tissue. The impediment to the return of blood by the hepatic vein leads to atrophy of the cells in the central portions of the acini and also to the formation of granular pigment, so that when examined microscopically, these portions of the acini are seen to consist of broken-down cells and granules of pigment. (Fig. 85.) At the peripheral parts of the acini the new interlobular growth is seen insinuating itself between the almost unaltered liver cells.

In the earlier stages of this affection the liver is often considerably increased in size from the large amount of blood which it contains. On section, it presents a peculiar mottled appearance, the centre of the lobules being of a dark red colour, whilst the peripheral portions are of a yellowish-white. Ultimately the organ may undergo a gradual diminution in size. This is due partly to the atrophy of the cells in the central portions of the lobule, and partly to the pressure of the interlobular growth. The interlobular growth tends to cause obstruction to the portal circulation, as in cirrhosis.

Mechanical Hyperæmia of the Lungs.—In the lungs long continued mechanical hyperæmia produces that peculiar induration and pigmentation of the organs which is known as *Brown Induration*. This condition most frequently results from stenosis and insufficiency of the mitral orifice. The alterations produced in the pulmonary texture consist in the first place of elongation and dilatation of the pulmonary capillaries, so that even in uninjected preparations the alveolar walls appear abnormally tortuous. The epithelial-like cells lining the alveoli also become swollen and ultimately multiply, and they are seen in large numbers covering the alveolar walls. (Fig. 86.) In some cases they may even accumulate

FIG. 86.



Brown Induration of the Lung. Showing the abnormal number of swollen epithelial-like cells covering the alveolar walls, the increase of connective tissue around the bronchus, *a*, and the large quantity of pigment. *b*. The alveolar cavity. × 200.

within the alveolar cavities. These changes are followed by an increase in the interlobular connective tissue, by the formation of large quantities of brownish-black pigment, and sometimes by a thickening of the alveolar walls.

Lungs in which these changes are at all advanced present a more or less uniform brownish-red tint, mottled with brown or blackish-coloured specks and streaks. They are heavier than natural, somewhat less crepitant, and upon squeezing them the pulmonary tissue is found to be denser and thicker than that of a healthy lung.

POST-MORTEM APPEARANCES OF HYPERÆMIA.—The post-mortem appearances presented by hyperæmic organs and tissues vary considerably. Very frequently, parts which were hyperæmic during life show no signs of it after death. If the blood does not coagulate rapidly it passes on into the veins, and thus the recognition of arterial and capillary hyperæmia very often becomes impossible. The effect of gravitation must also be taken into account in estimating hyperæmia. After death the blood naturally gravitates to the most dependent parts:—this is seen in the post-mortem congestion of the posterior portions of the lungs, and of the most dependent portions of the various coils of the intestine. The uniform redness of post-mortem staining again, must not be confounded with the redness of hyperæmia. In capillary and arterial hyperæmia, the colour is red, and the injection often presents the appearance of a capilliform network. If very intense, it may to the naked eye appear uniform, but a lens will always discover its capillary nature. When the veins are the seat of the hyperæmia the injection is called ramiform, and the colour is dark blue.

The anatomical peculiarities in the distribution of the blood-vessels will, however, materially affect the appearance of the hyperæmia. In the intestines it is often punctiform, being situated in the vessels of the villi; so also in the kidney, when its seat is the Malpighian corpuscles. A punctiform appearance may also be produced by minute extravasations of blood. If the hyperæmia is of long standing, the tissue becomes pigmented. This is often well seen in the stomach and intestines, also in the lungs.

CHAPTER XL.

THROMBOSIS.

THROMBOSIS is a coagulation of the blood within the vessels during life. This coagulation is owing to changes in the walls of the vessel itself, or to impeded blood-flow. The coagulum is called a *thrombus.* It may form in the heart, in the arteries, in the capillaries, or in the veins. It is much the most common in the last-named vessels.

Thrombi must be distinguished from the coagula that form after death, and also from those formed in the last moments of life, which are so commonly found in the cardiac cavities. Post-mortem coagula are soft, and are often divisible into two layers, coloured and uncoloured; they do not adhere to the walls of the vessel, and rarely completely fill its cavity. The clots formed in the heart just before death constitute a connecting link between post-mortem coagula and thrombi. They are usually more or less decolorized, and are firmer in consistence and more fibrinous than post-mortem clots. They are not firmly adherent to the cardiac walls, but are often so entangled amongst the columnæ carneæ, chordæ tendineæ, and papillary muscles, that they cannot be quite readily separated. They appear to be the result of the mechanical defibrination of the blood by the cardiac contractions just before death; the contractions not being sufficiently strong to empty the cavities, some of the blood remains behind, and becomes "whipped up" and defibrinated. These clots are most common in the right cardiac cavities, and they often extend some way into the pulmonary artery and aorta, from which, however, they can very readily be removed. They are met with most frequently in those cases in which death has taken place slowly, and in which there has been a gradual loss of power in the cardiac contractions. The proportion of fibrinogenous substance in the blood will also materially influence the extent of their formation.

A *thrombus*, or ante-mortem clot, is firmer, dryer, and more fibrinous than either of the preceding, and it is adherent to the walls of the vessel. Its characters, however, vary with its age, and with the circumstances under which it originates. When freshly-formed it is of a dark-red colour, and soft gelatinous consistence, closely resembling the post-mortem clot. It gradually becomes paler, dryer, less elastic, and more friable. If it is rapidly produced—as when the circulation is suddenly arrested in a portion of a vessel by the application of a ligature—the coagulum at once completely fills the vessel, and as it becomes firmer it maintains a more or less uniform structure. Thrombi, however, which have undergone a slow and gradual formation, are rarely thus uniform in structure, but are made up of numerous concentric layers, and so present a stratified appearance. This is owing to the coagulation taking place gradually upon the inner surface of the vessel, and to the white corpuscles adhering to the successive layers of coagulum. These corpuscles, from the property which characterizes them of adhering to one another and to the sides of the vessels, and especially to any porous substances with which they may come in contact, cohere with the fibrinous layers as they are deposited; so that ultimately the thrombus is made up of layers of fibrinous coagulum and white corpuscles more or less alternately and concentrically arranged. This gives to it a stratified appearance.

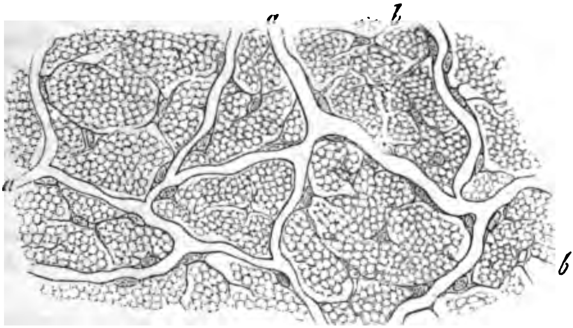
The thrombus may completely or only partially fill the cavity of the vessel. In most cases, however, when coagulation has commenced, it proceeds until the vessel is obstructed, and when once this has occurred, the formation of the thrombus continues to extend in the course of the vessel until it meets with a current of blood strong enough to arrest its progress. Its ultimate extent will thus mainly depend upon the vessel in which it is formed, upon the size and situation of the collateral branches, and upon the force of the circulating current. The direction in which the coagulation principally extends, whether in the arteries or veins, is consequently backwards from vessels of smaller to those of larger calibre; the formation of the thrombus continuing until it meets with a current sufficiently strong to restore the circulation, which in many cases is as far as the entrance of the next large collateral vessel. The end of the thrombus next the heart is rounded and conical in shape. (See Fig. 89 c.)

The thrombus when once formed either becomes *organized* or *softens*. The former is most frequent in the arteries, the latter in the veins and heart.

Organization.—This consists in the gradual transformation of the thrombus into connective tissue. A thrombus which is undergoing a process of organization gradually diminishes in size, it becomes more and more decolorized, firmer and more fibrous in consistence, its union with the wall of the vessel becomes more intimate, and ultimately it becomes converted into a fibro-cellular cord. These changes are principally owing to the white blood-corpuscles which it contains.

Soon after the formation of the thrombus the number of white blood-corpuscles which it contains becomes greatly increased, whilst that of the red ones diminishes. In a somewhat more advanced stage the red corpuscles almost entirely disappear, the clot becomes firm and homogeneous, and in addition to the round white corpuscles, numerous anastomosing spindle-shaped cells with oval nuclei make their appearance. (Fig. 87.) The intercellular material then becomes fibrillated, the walls of the vessel become infiltrated with cells, and numerous new blood-vessels are formed which intersect the thrombus in all directions. These vessels communicate with the cavity of the thrombosed vessel, and with its vasa vasorum. (Fig. 88.) The vascular fibrillated structure into which the thrombus has become organized gradually undergoes a process of atrophy and contraction, the new vessels disappear, and ultimately it becomes converted into a fibro-cellular cord. In some cases it becomes calcified, and thus forms a phlebolith.

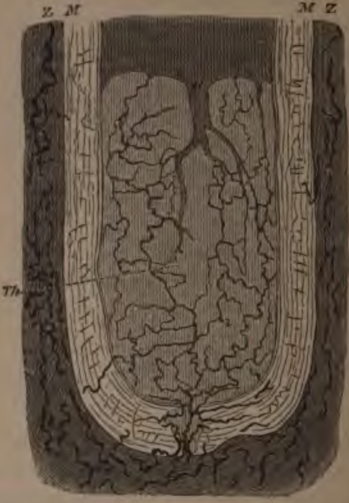
FIG. 87.



Section of an Arterial Thrombus Thirty-seven Days Old. *a.* New blood-vessels. *b.* White blood-corpuscles and anastomosing cells. (Rindfleisch.)

Respecting the source from which the large number of new cells which make their appearance in the thrombus are derived—it appears to be most probable that they originate from the white blood-corpuscles, and not from cells belonging to the walls of the vessel. Whether, however, they are all of them the offspring of the corpuscles which originally existed in the clot, or whether some of them may not be derived from other sources and subsequently penetrate it, is unknown. From these corpuscles the elongated connective tissue-cells are produced. The exact source from which the fibrillated intercellular material is derived—whether the intercellular coagulum itself fibrillates, or whether it disappears and the fibres are derived from the protoplasm of the cells, is uncertain.

FIG. 88.



Longitudinal Section of the Ligatured End of the Crural Artery of a Dog, Fifty Days after the Application of the Ligature. Showing the newly-formed vessels in the thrombus and their communication with the vasa vasorum. *Th.* Thrombus. *M.* Muscular Coat. *Z.* External coat and vasa vasorum. × 20. (O. Weber.)

Softening.—If the thrombus does not become organized, it usually undergoes a process of softening and liquefaction:—this is most common in the veins and heart.

It is probable also that in some cases the thrombus may become absorbed. The softening most frequently commences in the centre of the clot, and gradually extends towards the circumference. The thrombus breaks down into a soft pulpy material, which sometimes has the appearance of pounded cooked meat, and in other cases is distinctly puriform in character. Under the microscope it is seen to consist of albuminous granules, molecular fat, and more or less altered red and white blood-corpuscles. These changes in the clot are frequently owing simply to its disintegration, but in some cases it is probable that the thrombus may suppurate, and that owing to the proliferation of the white blood-corpuscles which it contains it becomes converted into true pus. The whole of the thrombus may thus become softened, or the process may be limited to the more central portions, whilst the external layers become organized. Very frequently as the older portions of the clot are becoming disintegrated and softened, fresh coagulation takes place at its extremities.

Causes.—The causes of thrombosis are of two kinds—those which lead to a retardation of the blood-flow, and those in which there is some abnormal condition of the walls of the vessels or of the blood.

1. *Thrombosis from Retardation of the Blood-flow* may result from—

a. Interruption or narrowing of the vessel.—This occurs after the application of a ligature. Coagulation commences at the point of contact, and extends as far as the first large collateral branches, thus permanently closing the vessel. The pressure exercised by tumours, cicatricial tissue, extravasations of blood, and the closure of a vessel by the impaction of an embolus, may in the same way by impeding or arresting the circulation cause thrombosis. General obstruction in the capillaries of a part also causes coagulation in the adjacent veins.

β. Solution of the continuity of the vessel.—The formation of a thrombus after the division or tearing of a vessel constitutes the means by which hæmorrhage is immediately arrested:—there must be either thrombosis or continuous hæmorrhage. In the arteries, the severed end of the vessel contracts and retracts within its sheath, coagulation commences around it and extends upwards as far as the first large collateral branch. In the veins, hæmorrhage is frequently arrested by the valves, and the formation of a thrombus will evidently depend upon the relative situations of the valves and collateral vessels. The hæmorrhage from the uterus after the separation of the placenta is arrested either by uterine contraction or by thrombosis.

γ. *Dilatation of the vessels, or of the heart.*—The most familiar example of thrombosis from this cause is that which occurs in an aneurism. The greater the amount of dilatation the greater is the retardation of the blood-flow. The coagulation commences at the sides of the vessel, and may extend until it completely fills the cavity. Coagulation from the same cause is not uncommon in the dilated plexuses of the prostate gland. In the heart, thrombosis is most frequent in the auricles. It usually commences in the auricular appendix, where there is very little propulsive power, and it may gradually extend into the auricular cavity. It is also met with in the ventricles, commonly commencing here between the columnæ carneæ.

δ. *Diminished cardiac power.*—This is a common cause of thrombosis in the veins. The coagulation commences just behind the flaps of the valves, from which it gradually extends into the cavity of the vessel. This appears to be owing to the force of the current not being sufficiently strong to completely open the valves, and the blood consequently stagnates and coagulates behind them. The crural and iliac veins, the venous plexuses of the back, and the cerebral sinuses, are the situations in which thrombosis from this cause is most frequently met with.

It occurs in the course of many chronic exhausting diseases in which the cardiac power becomes diminished, and has long been known under the name of "phlebitis." It is especially frequent in phthisis, cancer, and in chronic diseases of the bones and joints. The state of the blood, which often contains an excess of fibrinogenous substance, together with the quiescent condition of the patient, materially aid in causing the coagulation.

2. *Thrombosis from Abnormal Conditions of the Vessels or of the Blood.*

a. Causes in the vessels.—Any abnormal condition of the walls of a vessel may be a cause of thrombosis. When the wall becomes abnormal it acts as a foreign body and the blood coagulates upon it, and it may continue to do so until the cavity of the vessel becomes filled with coagulum. Thrombi produced in this way are consequently stratified. The walls of a vessel may become altered as the result of inflammatory processes, and inflammation was formerly regarded as the main, if not the only, cause of thrombosis; hence thrombosis in veins is frequently termed "phlebitis" at the present day. Inflammation of veins is certainly rare as a primary condition, although it not unfrequently results from the formation of a thrombus. When occurring primarily, inflammatory processes, both in the arteries and the veins, have their seat in the external and middle coats or in the deeper layers of the intima. They never commence in the lining membrane of the vessel: this only becomes affected secondarily. The vitality of the lining membrane becomes impaired as the result of the inflammatory process, and when this has occurred it acts as a foreign body, and thus there is a tendency for the blood to coagulate upon its surface. In other cases the lining membrane is completely destroyed, and the subjacent diseased tissues thus come into contact with the circulating blood, and in the same way cause the formation of a thrombus. Such inflammatory changes occur in the arteries, constituting the condition known as "atheroma," which, in the smaller vessels, may be a cause of thrombosis. In the heart they constitute endocarditis; and here also, as has been seen, coagulation may take place upon the abnormal surface of the inflammatory vegetations (see "Endocarditis").

The walls of a vessel may also become altered, and thus thrombosis result, from inflammation or gangrene of the tissues in which it is situated. The vitality of the vessel becomes destroyed and the blood coagulates within it; and by this means the occurrence of hæmorrhage is frequently prevented. The projection of new formations, as sarcoma, into the cavity of vessels, may in the same way cause the formation of a thrombus.

β. *Causes in the blood.*—The greater the proportion of fibrinogenous substance in the blood, the more readily will coagulation take place; hence all those conditions in which this substance is increased favour the occurrence of thrombosis. An excess of fibrinogenous substance, however, is probably never sufficient in itself to determine the formation of a thrombus; it can hence only be regarded as a predisposing cause. It is especially in those conditions in which the circulation is impeded from diminished cardiac power, that an increased tendency of the blood to coagulate becomes an important agent in producing thrombosis.

RESULTS.—The results of thrombosis comprise certain changes in the walls of the vessels, more or less obstruction to the circulation, and embolism. These must be considered separately.

1. *Changes in the vessels.*—More or less alteration in the wall of the vessel is an invariable consequence of the formation of a thrombus. When the thrombus undergoes a process of organization, it becomes, as already described, intimately united with the vascular wall. The latter in the first place becomes infiltrated with cells and

considerably thickened, but ultimately, together with the thrombus, gradually atrophies. It is when the thrombus softens and becomes disintegrated that the most important changes take place in the vessel. These changes are of an acute inflammatory nature, and appear to result from the irritating influence of the softened thrombus. They are most frequently observed in the veins, where softening is most liable to occur.

The walls of a vein within which a thrombus is softening are considerably thickened, so that the vessel more resembles an artery. The inner surface has lost its translucency, and is of a dead opaque colour. The vasa vasorum are hyperæmic. Under the microscope, the cells of the intima and of the middle and external coats are found to be considerably increased in number, and numerous leucocytes are seen infiltrating the different textures. In some cases small collections of pus are seen in the external coat. Similar changes are observed in the arteries.

2. *Obstruction to the circulation.*—The consequences of the obstruction to the circulation which results from the formation of a thrombus will depend upon the rapidity of its formation, the nature and size of the vessel obstructed, the situation and number of the collateral branches, and the force of the circulating current. When a thrombus forms in a vein of small size and there are numerous collateral vessels, as in the prostatic or uterine plexuses, the circulation is but little interfered with and no symptoms of obstruction result. If, however, the main trunk of a large vein becomes obliterated, as that of the femoral or iliac veins, the obstruction is followed by hyperæmia, the extent and duration of which will depend upon the facility with which the circulation can be restored by the collateral vessels. Thrombosis in the above-named veins frequently occurs in the latter stages of many chronic diseases, especially in phthisis; also in

the puerperal state, where it gives rise to the condition known as *phlegmasia dolens.* The formation of a thrombus here is followed by œdema and swelling of the limb, which becomes tense, elastic, and painful. In the early stage there may be some cyanosis, but this is usually quickly followed by a pallid whiteness of the surface. There is often more or less tenderness in the course of the vein, which feels enlarged, hard, and knotted, owing to the secondary inflammatory changes in its walls. At the same time there is frequently swelling and tenderness of the lymphatics, which may often be seen as red lines traversing the limb. Diffuse inflammation of the skin and subcutaneous cellular tissue may also occur. These changes are owing partly to the mechanical impediment to the circulation, and partly to the obstruction of lymphatics and to the secondary inflammatory processes in the vein and tissues which ensue. The circulation is usually ultimately restored; but if the impediment has been of long duration, the tissues become thickened, and the limb is left in a hard, indurated, and somewhat enlarged condition.

The formation of a thrombus in an artery is followed in the first place by anæmia of the parts supplied by it; the ultimate result will depend upon the facility with which the circulation can be restored by the collateral vessels. If the circulation be quickly re-established, as is usually the case, the vitality of the tissues may not become impaired; but if not, the part may undergo a process of molecular disintegration and softening, the softened tissue often being surrounded by a zone of hyperæmia which results from the attempt to establish a collateral circulation.

3. *Embolism.*—Portions of the thrombus may be carried away by the circulation, thus constituting embolism. This, which is the most important result of thrombosis, will be considered in the following chapter.

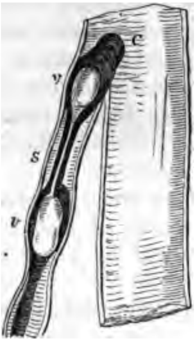
CHAPTER XLI.

EMBOLISM.

EMBOLISM is the arrest of solid substances circulating in the blood in vessels which are too small to allow them to pass. The solid substances are termed *emboli.* These are very various in their nature.

By far the most frequent source of emboli are thrombi, portions of which are carried from the seat of their formation by the circulation, and become arrested in distant vessels—thus constituting embolism. A thrombus may give rise to emboli in various ways. It may soften and break down, and if the lumen of the vessel be thus restored, its fragments become distributed by the blood-current. In those cases in which the thrombus does not fill the vessel, portions of it may readily be carried away by the blood passing over it. Perhaps, however, the most frequent way in which a thrombus gives rise to embolism is by its conical end being broken off by the current of blood from a collateral vessel. The formation of a thrombus, as already described, usually ceases opposite the entrance of a large collateral vessel, and if its conical end project a little way into the cavity of this vessel it may be readily broken off by the blood-current. (Fig. 89.) It is especially venous thrombi which give rise to embolism: the veins of the leg, the iliac, hypogastric, and jugular veins being amongst the most common sources. Emboli from cardiac thrombi are also exceedingly common; whilst those from arterial are the least frequent.

FIG. 89.



A Thrombus in the Saphenous Vein. Showing the projection of the conical end of the thrombus into the femoral vessel. *S.* Saphenous vein. *T.* Thrombus. *C.* Conical end projecting into femoral vein. At *v v*, opposite the valves, the thrombus is softened. (Virchow.)

Emboli may, however, originate independently of thrombi:—vegetations and calcareous or atheromatous masses separated from the valves of the heart, or from the inner surface of arteries; portions of new growths, as carcinoma, which having perforated the vessels, have been carried away by the current; parasites which have made their way into the interior of vessels; pigment granules, and other substances, may all constitute emboli.

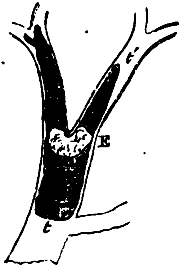
The emboli become arrested in the first vessels they meet with which are too small to allow them to pass: the size of the vessel will consequently depend upon the size of the embolus. They are often so minute that they pass into and become impacted in the smallest capillaries. The seat of impaction is usually at the bifurcation of the vessel, or where, from the giving off of branches, the calibre is diminishing rapidly. (See Fig. 90.) Thus emboli originating in the systemic veins or in the right cardiac cavities, will most commonly become arrested in the vessels of the lungs; those originating in the arteries, the left cardiac cavities, or the pulmonary veins—in the systemic arteries and capillaries, especially in those of the spleen, kidneys, and brain; and those originating in the portal venous system—in the hepatic branches of the portal vein. In some cases, however, the smallest emboli may pass through the capillaries of the lungs and become arrested in those of the kidneys, spleen, or other organs. Thus, with the exception of emboli originating in the portal vessels, the seat of arrest is the arteries or capillaries.

The emboli are usually carried in the direction of the main current; hence those carried by the aortic stream more commonly pass into the thoracic aorta than into the carotid and subclavian vessels, and into the left carotid and renal artery than into the corresponding arteries of the opposite side. Gravitation also influences the direction in which they are carried, especially those of large size which move somewhat more slowly than the blood-stream. Owing to this, they are more common in the lower lobes and posterior parts of the lungs than in the superior and anterior portions of these organs.

The embolus when arrested, may either completely or only partially fill the cavity of the vessel. If, as is frequently the case, the arrest takes place at a point of bifurcation, the embolus may partially fill both branches, allowing a small stream of blood to pass. This may break off portions of it, and so cause secondary emboli, which become impacted in more distant vessels. The amount of obstruction which immediately follows the arrest, will partly depend upon the nature of the embolus itself. If the embolus be from a soft, recently-formed thrombus, it will adapt itself to the cavity of the vessel, and so completely occlude it. If, on the other hand, it is irregular in shape and firm in consistence, as when derived from a calcified cardiac vegetation, it may not fill the vessel, but allow a small current of blood to pass it.

The arrest of the embolus and the consequent obstruction to the circulation, is followed by the formation of thrombi behind and in front of it, which extend as far as the entrance of the first large collateral vessels. (Fig. 90.)

FIG. 90.



Embolus impacted at the Bifurcation of a Branch of the Pulmonary Artery. Showing the formation of thrombi behind and in front of it, and the extension of these as far as the entrance of the next collateral vessels. *E.* Embolus. *t t'.* Thrombi. (Virchow.)

If the embolus does not completely fill the vessel, coagulum is deposited in successive layers upon its surface until the occlusion of the vessel is complete, and then the secondary thrombus extends, as in the former case, until it meets with a current of blood strong enough to arrest its progress. If the embolus is a portion of a soft thrombus, it will in most cases be impossible to distinguish it from the secondary thrombus which surrounds it. If, however, it is a calcareous mass, or a portion of an old thrombus, it may usually be distinguished from the more recent secondary coagulum. The changes in these secondary thrombi are similar to those already described as occurring in the primary,—comprising adhesion to the wall of the vessel, softening, and organization.

Results.—The results of embolism are of two kinds—those depending upon the mechanical obstruction to the circulation, and those produced by the irritating or infective properties of the emboli themselves. (See "Pyæmia.")

The first series of changes are those occurring in the walls of the vessel within which the embolus becomes arrested. If the embolus possesses no infective properties, being derived from a source where no putrefactive changes are taking place, it, together with the thrombus which it causes to form around and beyond it, simply becomes organized or reabsorbed, and the walls of the vessel become more or less thickened. If, on the other hand, the embolus is impregnated with unhealthy pus or with other putrid inflammatory products, it is very liable to cause inflammation and sloughing of the walls of the vessel within which it is impacted.

The most important changes, however, resulting from embolism are those which take place in the organ or tissue, the vessels of which have become plugged by the emboli. The first effect of the plugging of a vessel by an embolus, is the arrest of the circulation through it, and if the vessel be the main nutrient or functional artery, this is followed by the sudden cessation of the function and nutrition of the part. Thus, plugging of one of the larger arteries in the brain is followed by sudden loss of consciousness and paralysis (apoplexy); plugging of the pulmonary artery, by sudden asphyxia; and of the coronary arteries, by sudden paralysis of the heart. The subsequent changes will depend upon the structure of the organ, the arrangement of its vessels, and the facility with which a collateral circulation can be established. If the circulation be quickly re-established by the collateral vessels, the part recovers itself without undergoing any structural change, and its nutrition and functions are restored. If, however, this is not the case, and the nutrient supply is materially interfered with, either by the obstruction of the main vessel, of the principal branches, or of the capillaries themselves,—the death of the part must necessarily ensue. The interference with the circulation is in great measure dependent upon the thrombosis which occurs around the impacted embolus. The whole of the tissue thus cut off may suddenly die, or, as is more commonly the case, it undergoes a process of gradual molecular disintegration. This molecular death is in most cases attended by softening, and the softened tissues are usually surrounded by a zone of intense hyperæmia, which results from the stress which is thrown upon the collateral vessels. This zone of hyperæmia is very characteristic, and indicates at once the nature of the lesion.

The hyperæmia of the adjacent vessels, which results from the obstruction of the main or of several of the smaller branches, very frequently leads to the extravasation of blood. The distended capillaries give way, and the blood escapes and infiltrates the surrounding tissues. The tract of tissue within which the circulation has thus become arrested from the impaction of the embolus and the resulting thrombosis, and which is more or less extensively infiltrated with blood, is known as a *hæmorrhagic infarct.* These hæmorrhagic infarcts are very frequently met with, especially in the lungs, spleen, and kidneys. They are red masses of consolidation, and owing to the distribution of the blood-vessels, are usually wedge-shaped, the apex of the cone being towards the centre of the organ. If the circulation be not quickly restored, a process of molecular disintegration and softening commences in the central portions of the infarct. (Fig. 91.) The more complete the obstruction, the more vascular the tissue, and the less the vessels are supported, the greater is the amount of infarction, and the more rapid is the softening and disintegration that ensues.

Fig. 91.

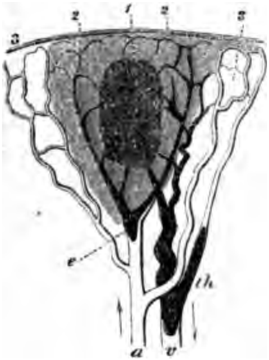


Diagram of an Embolic Infarct. a. Artery obliterated by an embolus (*e*). *v.* Vein filled with a secondary thrombus (*th*). 1. Centre of infarct which is becoming disintegrated. 2. Area of extravasation. 3. Area of collateral hyperæmia. (O. Weber.)

The subsequent changes which take place in the red infarct depend upon its size, upon the extent to which the circulation in it is interfered with, and upon the nature of the embolus which caused the infarction. If the infarct is small and the circulation still continues in parts of it, and if the embolus possesses no infective properties, the coagulated blood may gradually become decolorized, and the mass become partially absorbed or organized. The infarct then changes from a dark red to a brown or yellow tint, it becomes organized into connective tissue, and the whole gradually contracts, until ultimately a cicatrix may be all that remains to indicate the change. If, however, the infarction is considerable, and the circulation is completely arrested, a process of molecular disintegration and *softening* commences in the central portions of the tissue which may ultimately involve the whole mass, and the infarct then becomes converted into a pulpy granular material, which may subsequently dry up and become encapsuled. Lastly, if the embolus possesses infective properties, as when it is derived from a part where putrefactive inflammatory changes are going on, it sets up inflammatory processes both in the vessel within which it becomes impacted, and also in the surrounding thrombosed tissue. In this case the infarct rapidly becomes disintegrated, and is converted into a purulent liquid. This is the *embolic abscess.* (See "Pyæmia".) In all these secondary changes which take place in the infarct, its most external portions are surrounded by a red zone of hyperæmic tissue. This is exceedingly characteristic.

EMBOLISM IN THE BRAIN.

The impaction of emboli within the vessels of the brain is one of the causes of *cerebral softening.* The softening resulting from embolism is, for the most part, entirely dependent upon the obstruction to the circulation caused by the embolus and by the resulting thrombosis. It is rapidly induced and is usually attended by the extravasation of blood, and it constitutes the most frequent condition known as *acute red softening.* If, however, the interference with the circulation is slight, there may be no extravasation of blood and the process of disintegration may be more gradual, so that the softened portions are white in colour, and the condition then more resembles the chronic white softening already described as resulting from degeneration of the cerebral blood-vessels (see "Fatty Degeneration of the Brain"). The softened tissue will also be white in colour when one of the large vessels is obstructed, so that a large portion of one hemisphere loses its vitality. In such cases, only the pia mater and the most superficial layers of the cerebral substance may be hyperæmic. In almost all cases in which softening of the cerebral substance results from embolism, the embolus is arrested in one of the vessels beyond the circle of Willis, because here the circulation cannot be readily restored by the collateral vessels.

When the interference with the circulation is attended by considerable extravasation of blood, the softened portion, in the early stage, is either of a uniform dark red colour, or presents numerous red hæmorrhagic points. The softening is most marked in the centre, whilst the hyperæmia and redness may extend for some distance around it, so as even to involve the membranes. Under the microscope, the softened portion is seen to consist of broken-down nerve fibres, altered blood-corpuscles, granules of fat, and the large granular corpuscles which result from the fatty degeneration of the nerve-cells and of the cells of the neuroglia (see Fig. 5). The surrounding capillaries are dilated and filled with coagula, and the granular corpuscles envelope their walls. In a more advanced stage all trace of nerve structure is lost, the softened mass becomes decolorized, and passes from a dark red colour to a chocolate, brown, yellow, or even white. It may liquefy and form a cyst; more commonly, however, it gradually dries up, and a process of repair takes place by the growth of the surrounding neuroglia, which forms a fibrous network in the place of the softened tissue. This contracts, and ultimately a cicatrix with hæmatoidin crystals may be all that remains.

CHAPTER XLII.

THE PREPARATION AND MOUNTING OF SPECIMENS.

In this, the concluding chapter, it is proposed to describe very briefly the more common methods of preparing and mounting specimens for microscopical examination. It is not intended to give an account of those various and complex methods of investigation which are required for minute histological research, but merely to describe those more easy ones which suffice in the great majority of cases for the recognition of the structural alterations met with in disease. In order to be as brief as possible, those methods only will be described which the Author believes to be the most readily available and at the same time to yield the most satisfactory results. The subject will be treated under the following heads :—1st. *The Examination of Specimens whilst fresh;* 2nd. *The Hardening of Specimens;* 3rd. *The Making of Sections;* 4th. *Staining;* 5th. *Preservation and Mounting.*

THE EXAMINATION OF SPECIMENS WHILST FRESH.

Very much may be learnt from the examination of specimens in their fresh state before they have been submitted to any hardening process. The examination may be conducted either by making thin sections of the tissue with a Valentin's knife, or by cutting off a minute portion and tearing it to pieces with fine needles. The specimen prepared in either of these ways should be examined in glycerine. Thin membranous structures may be examined by simply spreading them out in a drop of glycerine placed upon the glass slide.

The method of making sections of organs whilst fresh with a Valentin's knife is an exceedingly easy and useful way of at once ascertaining in the post-mortem room the existence of the more marked structural changes. The knife should be well wetted with water, and then drawn *rapidly* through the substance of the organ. The section thus obtained is gently washed in water before being examined in glycerine. A rough examination of the liver, kidneys, and lungs is in this way readily made.

The muscular fibres of the heart and tumours may be examined by the process of teasing. This process, however, is usually more readily effected after the specimen has been kept in a solution of bichromate of potash in the manner to be hereafter described. In the examination of tumours, much may be learnt by gently scraping the freshly cut surface with a knife and examining in glycerine the elements which are thus separated.

THE HARDENING OF SPECIMENS.

In order to make a complete and satisfactory examination of diseased structures, it is in almost all cases necessary to submit them to a process of hardening. By this process they are so altered that fine sections of them can be made, and the sections are also rendered more fit for permanent preservation than are those obtained from tissues in their fresh state. Numerous substances have been employed as hardening agents. Those, however, which are the most generally valuable are *chromic acid*, *bichromate of potash*, and *alcohol.*

Chromic Acid.—Of all hardening agents this is much the most satisfactory and the one most generally applicable. It should be used in aqueous solution—strength one-sixth per cent. It is important to employ the solution in large quantities—from six to ten fluid ounces for each specimen. The tissue must be cut into small pieces—not much larger than a hazel-nut—before it is placed in the solution. The hardening is usually completed in from five to eight days. It is hastened by renewing the solution. If kept too long in the solution the tissue becomes brittle. All tissues which have been hardened in chromic acid should be placed in common alcohol for about twenty-four hours before sections are made.

Bichromate of Potash.—This agent is more gradual in its action than chromic acid, and produces less shrinking of the tissue. It is especially valuable for the hardening of kidney, blood-vessels, nerve-tissue, ovary, and some other structures. It is often advisable to commence the hardening with bichromate of potash and then to complete it in chromic acid or common alcohol. The bichromate is also valuable for the maceration of tissues which are to be examined by teasing—as tumours, muscle, &c. Its action tends to facilitate the isolation of the elements. The bichromate should be used in aqueous solution—strength one to two per cent. It penetrates more readily than the chromic acid, and consequently it is not necessary to use quite such small pieces of the tissue. The tissue must be kept in the solution from two to four weeks.

Alcohol.—This is most valuable as an agent for the completion of the hardening of tissues which have been previously placed in chromic acid or in bichromate of potash. The tissues should be kept in it one or two days. Some tissues, however, appear to harden better if they are at once placed in alcohol: amongst these are the lymphatic glands, spleen, and testis. Common alcohol answers for all these purposes. Lastly, alcohol must be employed for the hardening of all tissues which have been injected. For these absolute alcohol is necessary, as it is also for the completion of hardening of brain and spinal cord.

The Softening of Tissues.—Some tissues, as osseous structures, tumours which have become calcified, &c., require to be softened before sections can be made. This may be effected by placing them in the one-sixth per cent. chromic acid solution, to each six ounces of which three or more drops of concentrated hydrochloric acid have been added.

THE MAKING OF SECTIONS.

Although various instruments have been contrived for making sections, the one which answers best is a common razor, or a similar blade firmly fixed in a wooden handle. The usefulness of this instrument is much increased if the lower surface of the blade be ground perfectly flat, whilst the upper is made slightly concave.

Hardened tissues from which sections are to be made must always have first been placed in common alcohol, in the manner already described. In making the section the blade of the instrument must be kept well wetted with common alcohol, and the section when cut must be placed at once in the same liquid.

Imbedding.—Hardened tissues which are too small or too delicate to be held in the hand for the purpose of making sections, must be imbedded. The object of imbedding is to fix the tissue in some substance which can not only be readily held, but which can also be easily cut with the section-knife. Various substances are used for this purpose. Of these the one which is most generally applicable is a mixture of wax and olive oil. Equal quantities of pure white wax and olive oil should be warmed together and well mixed, and the mass when cold may be kept to be used as required. When a specimen is to be imbedded, a small case of paper should be made somewhat larger than the specimen. The edges of the paper can be secured with a little mucilage or with a pin. The mixture of wax and oil is then melted and the paper case filled with it. The specimen to be imbedded—which must have been removed from common alcohol—is now to be slightly dried on blotting-paper and immersed in the melted compound. The process of immersion requires a little care. The specimen should be placed upon the point of a fine needle, and as soon as the wax commences to solidify at the sides of the case, it must be dipped beneath the melted liquid so as to be completely covered by it. The needle must then be removed by giving it a gentle twist so as not to disturb the specimen. When the wax is cool the paper can be removed and the mass placed in common alcohol. Sections can be made from it when convenient.

STAINING.

When the section has been made and placed in common alcohol, in the manner described, it is usually advisable to stain it. The object of staining is to impart to the different portions of the tissue different shades of colour, so that its structure can be more readily recognised. The substance which is the most generally applicable for this purpose is *carmine*. In staining with carmine two methods may be employed:—the one consists in using a strong solution, so as to stain rapidly; the other in staining very gradually with a much less concentrated liquid. Of these, the method of gradual staining with weak solutions yields the most satisfactory results, inasmuch as by this means the differentiation of the tissue is rendered more complete than when the coloration is rapidly induced. The process of rapid staining with strong carmine is, however, the most convenient, and it yields, in most cases, sufficiently satisfactory results.

Gradual Staining with Weak Carmine.—The following is the method for gradual staining recommended by Dr. Klein:—

Take of—

Powdered Carmine	2 grammes.

Rub it up with a few drops of Distilled Water.

Add—

Liquor Ammoniæ fort.	4 cub. cent.
Distilled Water	48 cub. cent.

Mix together with a glass rod, and filter.

The solution to be kept in a stoppered bottle.

For staining, take one drop of the above solution, and add to it from nine to twelve drops of distilled water. Sections, which have been removed from common alcohol, to be placed in this from sixteen to twenty-four hours.

Rapid Staining with Strong Carmine.—To stain rapidly, the sections may be placed in the above strong solution of carmine without the addition of water. In this case the strong solution of carmine should have been kept exposed to the air for a sufficient length of time to allow the excess of ammonia to escape. It is consequently advisable to have two bottles of strong carmine solution—one for rapid, and the other for gradual staining.

The time required for rapid staining is from thirty seconds to five minutes. This, however, will vary very considerably according to the nature of the tissue to be stained. A knowledge of the amount of time which yields the best results will be readily learnt by a little practice.

The sections when removed from the staining solution must be washed for a few seconds in water containing one-quarter per cent. of acetic acid.

PRESERVATION AND MOUNTING.

When the section has been stained, it is ready to be prepared for mounting permanently. The two substances in which tissues are most commonly mounted are glycerine and Dammar varnish. Of these, the latter should be employed in all cases in which the preservation of the section is intended to be permanent. Many tissues, however, yield more satisfactory results when examined in glycerine; but they cannot be preserved in this liquid for any great length of time without undergoing some alteration.

The methods of mounting in Dammar varnish and glycerine must be described separately.

Mounting in Dammar Varnish.—When the section is to be mounted in Dammar—it having been already stained, and washed in the one-quarter per cent. acetic acid solution—it must first be placed in *absolute* alcohol for about a quarter of an hour. From the alcohol it must be transferred to oil of cloves, the superfluous alcohol having been first removed from the section by blotting-paper. In the oil of cloves it becomes, in a few seconds, quite transparent. The superfluous oil must be removed by blotting-paper, and the section is then ready for mounting in the Dammar varnish. If more convenient, it may be kept for one or two days in the oil of cloves before it is mounted in the Dammar. In order to make the specimen still more secure, a layer of the varnish may be placed round the edge of the covering glass a few days after the section has been mounted.

The following is the method for preparing the Dammar varnish:—

Take of—

Gum Dammar in powder ½ oz., and dissolve it in Turpentine 1½ oz. *Filter.*

Gum Mastic ½ oz., and dissolve it in Chloroform 2 oz. *Filter.*

Mix the two filtered solutions, and again filter.

Mounting in Glycerine.—When the section is to be mounted in glycerine no further preparation is necessary.

It is at once transferred from the one-quarter per cent. acetic acid solution to a drop of strong glycerine, which has been placed upon the slide. The edges of the covering glass must then be fastened down with some cementing liquid. The Dammar varnish answers exceedingly well for this purpose.

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